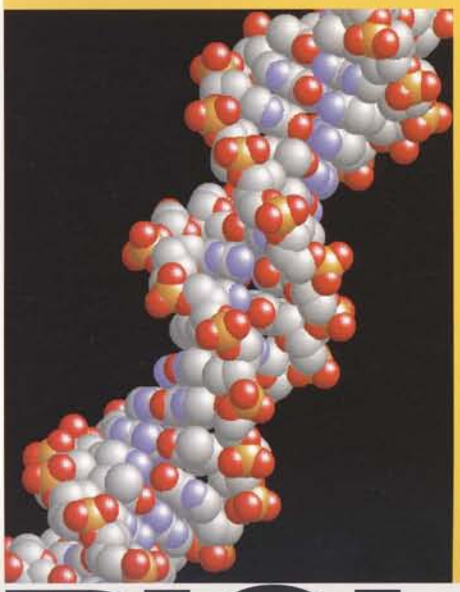

MICROBIOLOGY TODAY

QUARTERLY MAGAZINE OF THE SOCIETY FOR GENERAL MICROBIOLOGY VOLUME 26 NOVEMBER 1999

Into the next millennium...
Genomics & bioinformatics
The Edward Jenner controversy
SGM journals online – latest news
IUMS Congresses in Sydney

Contents

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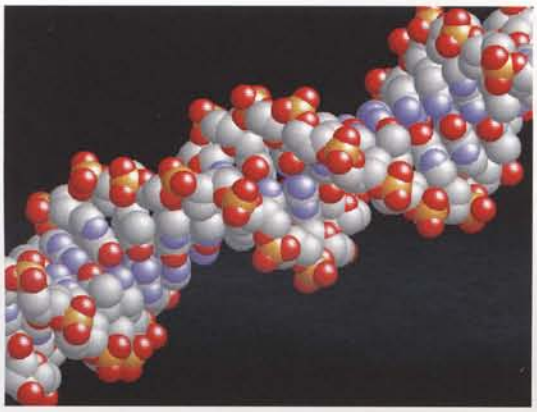


Above: DNA, the molecule at the centre of the modern science of genomics.

Image created by Bob Rastall, Department of Food Sciences, University of Reading, using RasMol software

Vol. 26, Part 4, November 1999

This issue of *Microbiology Today* is the last of the current millennium. In it we focus on a very hot topic – genomics – that offers exciting potential for solving microbiological problems in the next thousand years. Microbial sequencing is proceeding apace, with new genomes being announced almost monthly. Analysing the resultant wealth of information is down to bioinformaticists. In a range of articles, geneticists and computer experts describe the techniques and applications of microbial genomics and explore some of the exciting future opportunities that this knowledge will bring.

In a different vein, Allan Hamilton (p. 154) looks at the significance of microbes in the past 1000 years and offers some thoughts on the challenges facing microbiologists in future centuries.

Other topics covered include culture collections in Cuba (p. 188), The IUMS Congresses in Australia (p. 181) and a controversial book on who invented vaccination (p. 172).

These articles appear in addition to all the regular features and reports of Society activities.

Articles

Regular Features

Other Items

Microbiology at the beginning of a new millennium

Allan Hamilton

As we enter a new millennium, Allan Hamilton reflects on the impact of microbes on our lives and the challenges that lie ahead for microbiologists.

If millennium celebrations are to have any significance beyond the immediate and the trivial, then they should indeed celebrate events and achievements of the past 1,000 years, but do so in the spirit of looking forward to the opportunities and challenges of the future, built upon and made possible by these same earlier achievements.

How does microbiology respond to this clarion call?

It has to be said that the millennium is a peculiarly inappropriate time frame within which to examine the progress and development of microbiology. While a good case can clearly be made for marking the origins of microbiology with Leeuwenhoek and his 'animalcules' in the late 17th century, its true scientific study, largely in relation to medicine, only arose with Pasteur and Koch some 150 years ago, and within a larger environmental framework with Winogradsky and Beijerinck only in the early years of this century. The microbes themselves, blissfully unaware of man's concern or interest, have been busy originating life, and first creating then maintaining the biosphere for some thousands of millions of years!

The paradox inherent in these two very different time frames is paralleled by a striking dichotomy within microbiology itself in this year of 1999.

There is manifold evidence that microbiology lies at the heart of human affairs (MHHA); it has always done so and it always will. Yet as a subject discipline, microbiology remains largely misunderstood and even, to a significant extent, feared by the general public.

Biotechnology

Taking some examples of MHHA, one can reasonably start with '*biotechnology as the second oldest profession*'. There is evidence for the use of yeast in the brewing of beer in Mesopotamia as long as 6,000 years ago. In more general terms, the ability to harness microbial fermentation to produce a range of preserved and/or enhanced foodstuffs – beer, wine, bread, cheese, yoghurt – has always been one of the hallmarks of a settled society progressing along the road to what we would recognize as civilization. It is worth emphasizing here that advancement in these technologies was only made possible from the earliest times by the overt genetic modification of the starting materials through programmes of plant, animal and even microbial breeding.

Bread and blood

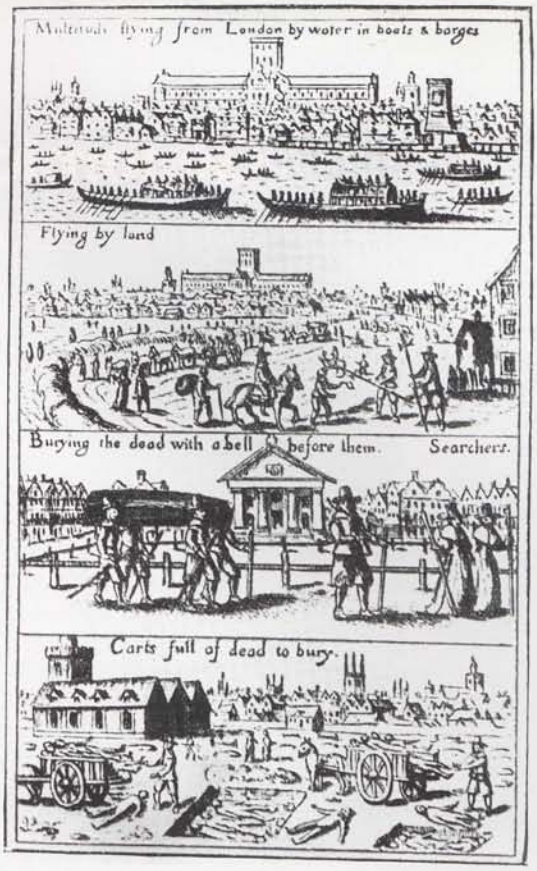
In all the talk of domes and parties, and indeed of the non-microbiological millennium bug, it seems often overlooked that the millennial time frame reflects one thing, and one thing alone; the origins of the Christian religion. Here again micro-organisms have a role to play; albeit a minor role and one involving a specific bacterium. The phenomenon of a red, or bloody, coloration of bread had been noted earlier by both Pythagoras and by Alexander the Great, but it was only with the Christian tradition of communion that the 'bleeding host' took on miraculous status and was seen regularly throughout the Middle Ages as tangible evidence of transubstantiation. It was in the early 19th century that an Italian pharmacist identified the pigment produced by a bacterium (which he named *Serratia marcescens*) as being the true nature of the 'blood'. *S. marcescens* will happily grow on a substrate such as bread which has been stored in a damp mediaeval church.

The Black Death

If one is looking for an organism whose impact on human affairs has been massive, and one which clearly demonstrates the complexity of the interdependence of microbes and man, then one need look no further than *Yersinia pestis*. Subsequent to the period of earlier Viking and Moorish invasions, Europe in the first centuries of the present millennium enjoyed a period of comparative social stability and growth, particularly in respect of commodity trading between different regions. These conditions gave rise to the development of trade routes and of fairs at their points of intersection, with a consequent increase in the free and safe movement of traders and their goods across the continent. By the beginning of the 14th century however, a combination of rising population and a period of cold wet weather with poor harvests, was imposing strains on the individual and collective welfare of the peoples of Europe. It was at this point that *Y. pestis* and the Black Death arrived, most likely from Asia along the Silk Route and into the Black Sea and Mediterranean sea ports of Southern Europe. The scale of human misery occasioned by this pandemic is difficult to grasp. From its appearance in 1347 in Messina and Marseilles, to its spread to Scandinavia, Poland and finally Russia in 1350/2, the plague killed approximately 30% of Europe's population of 75 million. Furthermore, sporadic outbreaks ensured that by the middle of the 15th century the continent's population was only half what it had been before the arrival of the pestilence.

Interestingly, the after-effects of the ravishes of the plague were very largely beneficial for the survivors. The remaining wealth and resources were spread across a smaller number of individuals; the shortage of manpower resulted in higher wages with a greater appreciation of specialist skills; and there was a conspicuous increase in spending, notably on luxury goods. These conditions enabled the seeds of the Renaissance to be planted.

Outbreaks of plague had, however, been known since as early as the 6th century, and even today it is not unknown in Africa and South America. The horrific scale of the 14th century Black Death was due to a combination of factors; the socio-economic conditions of the time, the lack of public health regulations and any appreciation of the aetiology of the disease, the absence of antibiotics or any other suitable treatment and, possibly, a mutation leading to a particularly virulent form of *Y. pestis*.



ABOVE:
Scenes in London during the plague of 1665. From a contemporary print in the Pepysian Collection.
COURTESY WELLCOME TRUST MEDICAL PHOTOGRAPHIC LIBRARY

The White Plague

Over the centuries *Mycobacterium tuberculosis* has probably been an even more effective enemy of mankind than the dramatic *Y. pestis*. Perhaps the most remarkable, and certainly the most sinister aspect of this saga is that around 1950, at least in the USA and Western Europe, tuberculosis had taken on the role of yesterday's disease through a combination of better living conditions, widespread application of population screening by chest X-ray and the development of effective drug treatment, most notably with streptomycin. Currently, however, we are faced with a dramatic re-emergence of tuberculosis as a major killer disease. There appear to be two major causes for this turnaround. AIDS, itself a leading candidate for the modern equivalent of the mediaeval Black Death, greatly increases the susceptibility of sufferers to secondary infection with *M. tuberculosis* and TB is very often the actual cause of death. Second, the great majority of new cases of TB are found to be already resistant to streptomycin and the few other known therapeutic agents. This latter situation arises from inadequate administration and supervision of drug treatment over the prolonged period necessary to combat the infection, with the consequent development and spread of drug-resistant *M. tuberculosis*. This is not a new problem (on a personal note, I helped the WHO compile statistics on the scale of the problem in Rio de Janeiro in 1962), but it is one that remains unresolved and largely intractable due to the numbers of patients affected, and the widespread need for treatment to be carried out either at home or in inadequate hospitalized facilities.

Future challenges and modern marvels

The emergence of new, and the re-emergence of 'old', pathogens, combined with the possible end of the antibiotic era, pose formidable microbiological problems for mankind in the years that lie ahead. But it would be quite wrong to focus exclusively on such negative aspects of MHHA. The positive gains to be won from the application of microbial organisms and technologies to industry and to the environment are potentially massive, as indeed will be the undoubted future successes in tackling human, animal and plant disease.

What is more, we have at the moment an unrivalled armoury of knowledge, techniques and understanding that make microbiology a subject of great intellectual excitement and one of huge practical utility. Molecular biology has matured into the study of genomics and proteomics which are already leading to greatly increased understanding of microbial physiology and pathogenicity. Similarly, genetic technologies have opened a Pandora's box with regard to microbial speciation and the origins and evolutionary development of life itself. Our appreciation of the true role of micro-organisms in environmental systems has taken on new significance with the identification of consortia, biofilms and surface growth, and our horizons have widened with the study of the nature of the interactions between microbial and physical/engineering systems. Although not 'Orange', the future is bright!

Public perceptions

But the paradox of the disparate views of science between scientists and the general public remains, and the removal of that disparity in respect of microbiology must be the single major objective for all right-minded microbiologists as we enter the next millennium. The difficulties take two forms; one of knowledge, the other of perception. While it is undoubtedly true that the advancement of science in general, and of microbiology in particular, depend on a great deal of specialized technical knowledge, the essential information can be made available to the layman with skilful reportage and responsible journalism. The clue to the success of this communication, however, lies in the readiness of the public to accept the truth and validity of the message being presented. It is this which has been at least partially eroded in recent years by a combination of irresponsible and sensation-seeking journalism, and the growth of a climate of opinion that demands an easily identifiable individual or organization against whom can be laid the blame for any and every circumstance that carries with it an element of risk. Such an approach to the challenges and opportunities of the next millennium represent short-termism and Nimby attitudes at their worst, totally at odds with man's progress in previous centuries and quite inimical to all possible future advancement. It is a legacy we must not carry forward with us into the next millennium. As microbiologists, therefore, perhaps our greatest challenge for the future lies not so much with advancing our chosen subject as with making it more truly accessible to the general public in all its intellectual vigour and beneficial practicality.

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Genomics and bioinformatics

Simon Baumberg

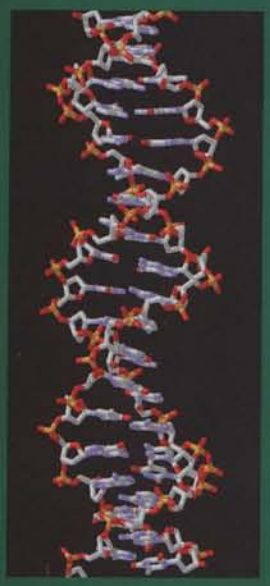

IMAGE CREATED BY BOB RASTALL, DEPARTMENT OF FOOD SCIENCES, UNIVERSITY OF READING, USING RASMOL SOFTWARE

Microbiology has never been the same since 28 July 1995. That was the publication date of the issue of *Science* containing the first complete bacterial genome sequence – indeed, the first complete sequence for any free-living organism. The creature in question, the pathogen *Haemophilus influenzae*, was soon followed by *Mycoplasma genitalium*, the archaeon *Methanococcus jannaschii*, the yeast *Saccharomyces cerevisiae*, *Helicobacter pylori*, *Escherichia coli* and *Bacillus subtilis*. As of 2 September 1999 the web pages of The Institute for Genome Research, where the pioneering *H. influenzae* sequence was determined (http://www.tigr.org), give 24 microbial genomes or chromosomes (16 bacterial, 5 archaeal and 3 eukaryotic, including single chromosomes for *Plasmodium falciparum* and *Leishmania major*) as completed and 91 entries as in progress.

Assembling, documenting and curating megabases of DNA are the first tasks of bioinformatics. The next stage involves scanning the sequence for open reading frames (ORFs) which are likely to encode proteins. This involves looking for extended reading frames lacking 'stop' triplets (finding functional RNA molecules requires searching for homologies with known examples). Then the polypeptide sequence derived from each ORF is used to probe the composite protein database, allowing recognition of homologies which may extend over part or all of the unknown sequence. This crucial stage may permit an ORF to be recognized as encoding a protein whose exact function is known, or as containing a domain generic for a certain class of proteins, or as homologous to another protein of unknown function – or it may show no recognizable relationship to any protein. In the case of *H. influenzae*, of the 1,743 identified ORFs, roles could be assigned to 58% on the basis of homology with polypeptide sequences of known function and 20% matched hypothetical polypeptides already in the database (i.e. whose sequence, but not function, was known); this left just 22% without a database match.

Such results can in themselves be of great interest. For instance, it is clear that obligate commensals or pathogens like *H. influenzae* have dispensed with much of their biosynthetic capacity, having lost many genes involved in biosynthesis or its regulation. Observations of this type can pose questions whose answers will require the integration of molecular studies with ecology. The partially completed *Streptomyces coelicolor* sequence allows the inference that although this organism has a genome of only c. 8 Mbp in comparison to the c. 13 Mbp of *Saccharomyces cerevisiae*, the mean size of ORF (1·2 kbp vs 2·2 kbp for the latter) would give >7,000 genes for the prokaryote but <6,000 for the yeast. What extra genes does *Strep. coelicolor* possess to account for the difference from *E. coli* with its 4,000 genes? The answer seems to be a multiplicity of ABC transporters and two-component regulatory systems, which one may conjecture are needed for its complex developmental cycle.

Information breeds the need for more information, and if Bill Gates didn't say that (he probably didn't), he should have. It is clearly not enough to guess at the function of the thousands of genes with limited or no homologies; their functions must be determined as far as possible. Hence, some genome projects, notably those for *S. cerevisiae* and *B. subtilis*, have been followed by 'analysis of function' projects. In these, consortia are formed to make a knock-out mutant of every gene, while others examine these phenotypically according to a pre-determined scheme, allowing further inferences to be made about each gene's function. (There are ways of allowing for the fact that many genes will encode essential functions.) Going further down the functional analysis road, methods have been or are being devised to obtain complete catalogues, termed the 'transcriptome', 'proteome' and 'metabolome', respectively, of all RNA molecules transcribed within an organism, all proteins produced and all non-informational macromolecule compounds present, in all cases under particular conditions. The latter approaches will eventually reveal what genes are expressed and to what extent, and how the metabolism of an organism changes according to conditions. For instance, it will be possible (also by means of *in vivo* methods such as IVET techniques) to ascertain which genes of a bacterial pathogen are switched on only during infection.

It will not have escaped the notice of *Microbiology Today*'s readers that substantial investment in genome projects has come from industry, especially pharmaceutical companies. Why is a return expected on this? One answer is that the protein product of a novel gene in a pathogen, if its function is shown to be essential during infection, could represent a target for new antibacterial agents. The protein could then be used as a target in drug screening, or its structure could be determined, e.g. by X-ray diffraction, and potential low molecular weight inhibitors then predicted.

Returning to basic science, we remember the drosophilist Dobzhansky's dictum *'nothing in biology makes sense except in the light of evolution'*. Genome sequences give us the results of evolution in the most complete and direct form. In the teeming data there must be clues as to, for instance, where the archaea stand in relation to pro- and eukaryotes, and how and in what sequence the various protist groups separated from each other. For the moment, obvious approaches are enough to provide us with vast amounts of work and novel information. The challenge of the coming years will be to find ever subtler questions and ways of answering them.

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Genomic analysis methods

James O. McInerney & Kenneth H. Wolfe

When all the contigs have been joined and all the sequence ambiguities have been ironed out, the time comes in any genome sequencing project when it is necessary to annotate the completed sequence. Even scientists who are not directly involved in large-scale sequencing may have an interest in genome annotation and analysis, because bacterial genome sequences are now often released in a preliminary form – finished but not annotated, or even unfinished – many months before they are published. Obviously, annotation is not a trivial undertaking, but rather one that requires the use of an extensive range of bioinformatic skills. The focus of the project moves from the 'wet lab' with its gels, sequencers and PCR machines to the 'dry lab' of hardware, software and algorithms.

The sequencing project could also be said to move from the hard facts (the exact DNA sequence) to the softer inferences: attempting to identify potential open reading frames (ORFs), to assign homologies from sequence similarities, to identify motifs and fingerprints, to study codon usage patterns, to find genes that have been acquired recently through lateral transfer, and so forth. It may sound as though a lot of hand-waving is involved, but with the recent development of exquisitely sophisticated algorithms many of the heuristic elements have been removed. At first glance, a completed microbial genome sequence appears to be an unruly and undisciplined assortment of the four nucleotides. However, a careful analysis, combining a sound knowledge of microbial biochemistry with good computational assistance can provide a surprising insight into the macromolecular architecture of a completed genome.

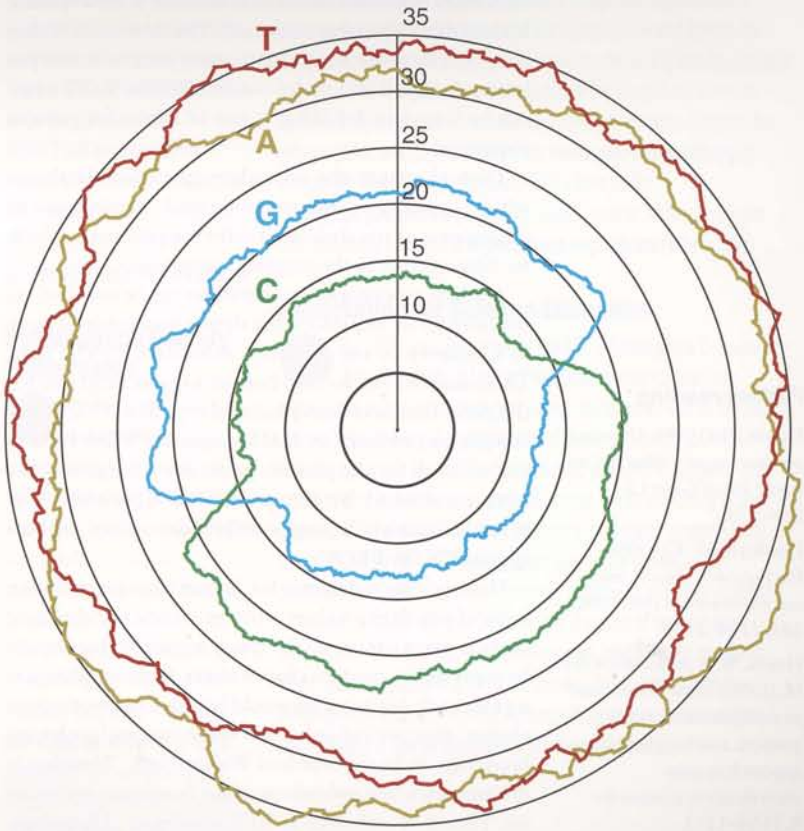
Finding the genes

It is an easy process to identify potential protein-coding genes, but it is infinitely more difficult to identify those that are *de facto* protein-coding. We can simply look for potential start codons and stop codons. The result of this type of simplistic approach is a collection of ORFs (potential genes) of varying sizes. Rules of thumb can then be applied, for example the observation that real genes almost never overlap by more than a few bases, and that large ORFs are extremely unlikely to be spurious (the threshold chosen might be 100–200 amino acids, depending on base composition). It is advisable, however, to do database searches (see below) with the complete set of all ORFs in the genome, before any other prediction methods or length limits are applied, because the clearest indication that a gene exists is a strong match to a gene from another species.

This approach will find many genes but will leave holes in the genome where there may be ORFs that are real genes without homologues. We need robust methods for eliminating the unlikely candidates while retaining those that might reasonably be expected to encode a functional peptide. The most frequently used gene prediction method is the non-homogenous hidden Markov model (HMM) method, described by Mark Borodovsky. First, a training set of 'known' genes and 'known' non-coding regions must be supplied. These sets are then used to define frequently used and infrequently used oligonucleotides and frequency matrices are constructed. These matrices are used in a moving window analysis of the genome to find regions with oligonucleotide frequencies that correspond favourably with those in the pre-defined matrices. In this way, it is possible to predict the state of each region of DNA as coding or non-coding, independent of ORF content. HMMs are quite efficient at identifying real genes but can have difficulty deciding whether to include or exclude regions between alternative possible start codons at the 5′ ends of genes. Current HMMs are being developed with the goal of improving the reliability of recognizing the correct start codon in a gene.

Database similarity searching

One of our first ports of call when trying to make sense of a new genome is at the sequence collections. These began in the early 1980s and have never failed to double in size each year. Sequence collections come in a variety of guises. There are repositories such as GenBank or EMBL,



BELOW:
Fig. 1. Variation in base composition around the *Chlamydia trachomatis* genome. The radar plot shows the frequency of the four nucleotides at synonymous (third) codon positions, calculated as a moving average from synonymous sites within a window of 40 kb of genomic sequence. In most sequenced eubacteria the leading strand is relatively rich in G+T, and the lagging strand rich in A+C, so in *C. trachomatis* the origin and terminus of replication are probably at about 8 and 2 o'clock, respectively, in the plot.

Table 1. Useful websites

GenBank	
	http://www.ncbi.nlm.nih.gov
BLAST	
	http://www.ncbi.nlm.nih.gov/blast
EMBL	
	http://www.ebi.ac.uk/embl
SWISS-PROT and TrEMBL	
	http://www.ebi.ac.uk/swissprot

which accept almost all sequences submitted to them and make them available to the public in an unaltered form, either immediately or after a short holding time requested by the sequencer. These repositories are the largest and most up-to-date sources of DNA and protein sequences. The downside to using these repositories concerns the deliberately light curatorial process and the large amount of internal redundancy (duplicate sequences or near-duplicates). In addition, sequence annotation can be quite spartan and there is no consistency across repository entries in relation to descriptive terminology and the use of keywords because these are supplied by individual authors.

A sequence database, on the other hand, is a curated, non-redundant collection of sequences, with a certain amount of consistency in nomenclature (both for the taxa and the molecules) and keyword usage. Databases such as SWISS-PROT are annotated to a high level and each entry contains a substantial amount of the available knowledge about that molecule. The downside is that there is a large backlog of sequences that have not yet been annotated and so are not in SWISS-PROT (they can be found in TrEMBL, a sort of limbo for protein sequences).

Then there are the secondary specialist databases which usually contain annotated sequences or alignments or use dedicated software products to look for 'fingerprints' in the supplier's sequence.

All these repositories and databases can be searched via the internet for sequences that show a reasonable amount of similarity to the sequence submitted by the user. These searches can be used both to suggest functions for the genes that have been predicted (e.g. BLASTP searches of proteins predicted by HMMs against SWISS-PROT) and to check for any possible genes or pseudogenes that were overlooked by the prediction algorithm (e.g. BLASTX searches of supposedly non-coding regions against SWISS-PROT).

Having found a database hit, we can then decide on the basis of similarity values whether or not the database entry is more similar to the query sequence than would be expected by random chance alone. If the similarity is significantly higher than would be expected by random chance, then we can infer that these two molecules are homologous. In the words of Walter Fitch, *'Homology is like pregnancy, two molecules are either homologous or they are not. There is no such thing as 70% homologous'*. Homology means descended from a common ancestor and the term was coined by Richard Owen in 1843, who defined it (for the purposes of morphological systematics) as *"the same organ under every variety of form and function"*. In molecular terms, we define two genes as being homologous if we can infer that they arose from a common ancestor. If they show a higher degree of similarity than would be expected by chance, then it appears to be reasonable in most cases to make the leap of faith and assign both sequences to the same homologous superfamily. Molecular homology can be subdivided into orthology and paralogy: human insulin and mouse insulin are orthologues (they diverged due to species formation), while human α- and β-globin are paralogues (they diverged due to a gene duplication within a species).

The process of trawling through sequence collections looking for sequences of high similarity can be quite rewarding and usually results in many ORFs being assigned to a homologous superfamily. In many cases, it may even be possible to infer a specific function for the ORF, although this must be done with great care because of the problem of 'annotation transfer'. Many genes in GenBank are annotated as having a particular function, whereas in fact this is just an inference based on sequence similarity to some other organism where the wet-lab experiments have been done. When these 'friend of a friend' chains of inferred function become too long, the inference becomes unreliable. A related problem is that any mistake in the annotation of a gene's function in one genome sequence (e.g. a poor judgement call by an author) can become perpetuated by annotation transfer to other genomes and then becomes very difficult to clear up.

When there are no similar sequences

In every completely sequenced genome there are some probable genes that cannot (even tentatively) be assigned a function on the basis of sequence similarity. Some of these fall into gene families whose sequences are conserved but where a function has not yet been discovered for any member of the family. Other ORFs without homologues must be incorrect predictions and not genes at all. A third group are 'orphans' – genes without families. A combination of evolutionary rate and time since separation from the most recent common ancestor may conspire to make sequences that are homologous appear to be unrelated in sequence. Alternatively, a homologue of the ORF in question may exist somewhere in nature but never have been sequenced before. The question then arises *"What, if anything, do these ORFs encode?"*

Plainly, this question represents something of a holy grail in molecular biological terms. If it were possible to assign functional information to ORFs in the absence of database similarity, then we would be able to make a substantial contribution to the understanding of the biology of every completed genome. Progress in this area

Further reading

Dujon, B. (1996). The yeast genome project: what did we learn? *Trends Genet* 12, 263–270.

Doolittle, W. F. (1999). Phylogenetic classification and the universal tree. *Science* 284, 2124–2129.

Hayes, W. S. & Borodovsky, M. (1998). How to interpret an anonymous bacterial genome: machine learning approach to gene identification. *Genome Res* 8, 1154–1171.

has been made recently by using DNA microarrays to study expression patterns, particularly in yeast. Groups of genes involved in the same biochemical pathway or physiological process tend to be co-regulated. Consequently, if an ORF's expression pattern under a wide variety of conditions groups it with several other genes, all of which are involved in some pathway, the ORF is also likely to be involved in this pathway. This approach can be used to generate hypotheses that can be tested in the lab, but is not yet at the stage where predictions can be made infallibly.

Other genomic patterns

There are other patterns that can be found in completed bacterial genomes. For instance, when the completed sequence of *Mycoplasma genitalium* became available, it was possible to find an unusual wave of base composition heterogeneity around the genome. This wave of base composition variation has a knock-on effect on codon usage within the genome. As yet, the reason for this peculiarity remains unknown. In the spirochaetes *Borrelia burgdorferi* and *Treponema pallidum* there is another unusual phenomenon. There is a significant difference in base composition between the leading and lagging strands of DNA replication and usage of most of the synonymously variable codons is significantly different between the two strands. This time there is a clear explanation for this base composition bias and it is related to replication.

Some extraordinary claims concerning lateral gene transfer have been made since complete and nearly complete genomic sequences have been made available. It has been suggested, on the basis of nucleotide composition analysis, that a very large portion of the *Escherichia coli* genome has been acquired by horizontal transfer since it shared a common ancestor with *Salmonella*. This is a difficult hypothesis to test using an independent dataset, although denser sampling of taxa, combined with phylogenetic inference does have the potential to clarify the issue. Should it prove that these figures are a reasonable estimate of the levels of lateral transfer, there are considerable implications for molecular biologists and evolutionists to reflect upon.

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Funding

MRC/Royal Colleges of Physicians & Pathologists Training Fellowships in Clinical Infection and Medical Microbiology

The aim of these Fellowships is to encourage promising young clinicians who are pursuing clinical training under RCP or RCPath schemes to undertake a period of research training in clinical infection and medical microbiology which involves work in the clinic as well as in the laboratory. Applications are particularly encouraged from those intending to obtain joint accreditation under the new RCP/RCPath training scheme in medical microbiology and virology and infectious diseases. The Fellowships provide the opportunity for specialized or further research training in relevant fields within the UK, leading to the submission of a doctoral thesis. There will be two awards available under the scheme in the 1999/2000 session and the closing date for the competition is **26 January**. Further details can be obtained by e-mail from **fellows@headoffice.mrc.ac.uk**

Pathological Society Fellowships

The Pathological Society sponsors fellowships to enable members of the medical and scientific professions working in the UK or Ireland in experimental and/or pathologically or microbiologically related research to travel to other institutions for periods of up to 12 months to learn new techniques of value in their research. Deadlines: **1 October** and **1 March**. Application forms and details are available from 2 Carlton House Terrace, London SW1Y 5AF (**www.pathsoc.org.uk**).

Research

Microbes in Norwich (MICRON)

A new website has been created to unite microbiological research in Norwich, UK. This brings together information on over 25 group leaders working within the University of East Anglia, the John Innes Centre, the Institute of Food Research and the Sainsbury Laboratory who have research interests in numerous aspects of microbiology. The site features an organism-based structure containing introductory information on all the microbes under investigation. The site also contains listings of microbiology seminars and meetings in Norwich and the surrounding area. The URL for MICRON is **http://www.jic.bbsrc.ac.uk/hosting/microbes/index.html.** For more information contact either Mike Merrick (**mike.merrick@bbsrc.ac.uk**) or Gavin Thomas (**gav.thomas@bbsrc.ac.uk**).

Education

American Society for Microbiology Resources

Our colleagues in the States have been busy expanding the range of resources that they produce to promote microbiology as a subject and as a career. A particularly exciting project, as part of the Microbial Literacy Collaborative, is the production of *Unseen Life on Earth*, a comprehensive new video series and television course. A four-part documentary is to be screened on national television in America this autumn and the video series will be launched in January, covering Microbial cell biology, Microbial genetics, Integrating themes, Micro-organisms and the environment and Micro-organisms and human life. Books and other resources to complement the series will also be available from the ASM next year. Different aspects of the project are aimed at specific audiences such as schools and colleges, distance learners, the general public and libraries. Check out **www.microbeworld.org** or contact the SGM External Relations Office for a leaflet (**info@socgenmicrobiol.org.uk**). Details of other ASM educational resources may be found at **www.amusa.org/edusrc/edu4c.htm**

Association for Science Education

The 2000 annual meeting of the ASE will take place 6–8 January at the University of Leeds. Thousands of science teachers, technicians and advisers from many other countries as well as the UK will attend. There is a very full programme of lectures, workshops, INSET courses and visits. Over 200 manufacturers, publishers, suppliers and organizations providing services to education will be exhibiting at the meeting. SGM and MISAC will be there on a joint stand, promoting the theme 'Building up . . . Breaking down' (microbial growth versus decomposition) and distributing posters, factsheets and other materials. SGM and the NCBE will also be launching the pack of fermentation activities for 16+ that has been developed by John Schollar and Bene Watmore with sponsorship from the Society. If you require further information or a copy of the ASE Advance Programme, please contact **Janet Hurst** or **Dariel Burdass** at Marlborough House.

What sequence homology tells us about the functions and origins of viral genes

Andrew Davison

Sequence homology tells us how genes are related to each other and what their history is. Many viruses – most strikingly the large DNA viruses – have captured genes from their hosts, and many may even have recycled some to new uses. Andrew Davison depicts gene capture as a key component of viral evolution.

Scientists are often characterized as those who like to explain simple things in complex terms – sometimes so complex that it seems their own understanding petered out some time ago. But this is a misrepresentation. It may be that biological phenomena are ultimately too complex to understand fully, but the urge to explain complicated systems in simple terms is an irresistible human, and therefore scientific, trait. The search for patterns is fundamental to research – life's complicated enough.

Shared heritage

The evolutionary concept of biological systems implies a shared genetic heritage. That such a heritage exists, even between organisms with strikingly dissimilar phenotypes, has become glaringly obvious in the age of genome sequencing. This offers a huge simplification to understanding gene function across wide ranges of organisms: the role of a gene in one organism may be deduced from that of a related gene in another, providing that function is known. The principle behind this is that conservation of protein function results in conservation of structural motifs. This is most readily detected as amino acid sequence similarity and, depending on mutation rate and the time that has elapsed since divergence, sometimes as nucleic acid sequence similarity.

This aid to tracking down gene function applies to viruses as much as it does to their hosts. In general, viruses tend to change faster than their hosts (from one to six orders of magnitude faster), thus placing a greater emphasis on amino acid, rather than nucleic acid, sequence comparisons as the primary means of detecting similarity. This, in addition to the lack of viral fossils (except, in a special sense, retroviruses) and consequent difficulties in assigning evolutionary timescales, makes it more difficult to look as far back in time along viral lineages as is possible along host lineages. Whichever computer program is used for detecting related proteins, all eventually reach a 'grey area' where relationships become tenuous and their interpretations speculative. Analyses can be pushed further by searching for motifs conserved between a set, rather than a pair, of proteins, but even then uncertainty dominates at some point. Given the evolutionary rates of viruses, it is in this ocean that information on distant origins is located; unfortunately, these are also waters where red herrings abound.

Captured genes

In responding to selection pressures, it appears that viruses have utilized all available means for generating diversity. Their genomes have been subject to gradual processes of mutation – nucleotide substitution and associated small insertions and deletions, generation of domains or entire genes *de novo*, gene duplication followed by functional divergence, gene fusion, gene loss, gene translocation, recombination or reassortment between related viruses and capture of cellular or other viral genes. It is in the category where viruses appropriate cellular genes (in large DNA viruses probably via RNA intermediates), that the search for genetic origins by detecting similarity has come into its own. The fact that many ancestral viruses appear to have captured cellular genes has led to their description as 'molecular pirates'. Whether this anthropomorphism, which envisages a virus as 'Cut-throat Jake' or one of his gang on the lookout for an opportunity to rob the unsuspecting cell of a handy gene, is more accurate than that of a virus as a 'Borrower' who can pinch a gene and modify it for another purpose, we do well to remember that viruses lack motive. Moreover, in that viruses are constantly intimate with the organism they infect, hosts are also shaped by their viruses. It is on this stage that the delicate dance of coevolution succeeds when it results in survival of virus and host.

Gene capture as a mechanism of adapting to the host has been most abundantly seen in the larger DNA viruses, such as the poxviruses (with their cytoplasmic lifestyle) and, to a lesser extent, the herpesviruses. This is likely to have been promoted by the ability of larger viral genomes to incorporate significant amounts of additional sequence and still be packaged into infectious virus particles, and by the fact that such viruses face a hostile array of sophisticated cellular defences, particularly those involved in immunity. Nevertheless, gene capture has been utilized in many viral lineages and has occurred throughout viral evolution. Many viruses, for example, encode a DNA or RNA polymerase and a helicase, functions that are likely to have been required at early stages in viral evolution and are assumed to have been captured. Genes whose products are involved in nucleotide biosynthesis and DNA repair are characteristic of larger DNA viruses. Examples include thymidine kinase (of various origins), thymidylate kinase, guanylate kinase, deoxyuridine triphosphatase, ribonucleotide reductase, thymidylate synthase, dihydrofolate reductase, uracil-DNA glycosylase, DNA methyltransferase, topoisomerase and DNA ligase. Other captured genes include those encoding subunits of RNA polymerase, poly(A) polymerase, mRNA capping enzyme, phospholipase, sialidase, haemagglutinin, protease, protein

LEFT and OPPOSITE PAGE: 'The fact that many ancestral viruses appear to have captured cellular genes has led to their description as '*molecular pirates*'. CARTOONS OF *CAPTAIN PUGWASH* AND *CUT-THROAT JAKE* ARE TAKEN FROM *PUGWASH THE SMUGGLER* BY JOHN RYAN, PUBLISHED BY THE BODLEY HEAD, AND ARE REPRODUCED WITH THE PERMISSION OF THE RANDOM HOUSE GROUP LTD

kinase, protein kinase inhibitor, protein phosphatase, semaphorin, profilin, 3β-hydroxysteroid dehydrogenase, glutaredoxin, phosphoribosylformylglycinamidine synthase and superoxide dismutase.

In addition to genes involved in nucleotide synthesis and DNA replication or repair, large DNA viruses have captured genes whose products presumably function in subverting cellular processes, including modulators of apoptosis and various zinc-finger proteins with probable regulatory functions. Poxviruses and certain herpesviruses (notably human herpesvirus 8, implicated as the causative agent of Kaposi's sarcoma) also have impressive repertoires of genes whose cellular counterparts are involved in immune function: chemokines, chemokine receptors, growth factors, interferon regulatory and resistance factors, MHC antigens, proteins involved in the complement pathway and other proteins that may function in immune recognition in as yet poorly understood ways.

Recycling

The picture is one of ready incorporation of potentially useful cellular genes into the genomes of large DNA viruses. In attaching a proper sense of timescale to gene capture processes, however, it is important to bear in mind that fixation of captured genes into a lineage is very rare, and that most such events occurred in the distant past. Divergence of captured genes from their more slowly evolving cellular parents, in some cases accompanied by gene duplication, can lead to functional diversification. For example, a component integral to a cellular process can be released from regulatory constraints in the viral context or can even be developed into a means of inhibiting that process. Moreover, divergence can ultimately result in loss of the original function and gain of a new one. It appears that this may be the case for deoxyuridine triphosphatase and ribonucleotide reductase in the cytomegaloviruses (β-herpesviruses) and for superoxide dismutase in the poxviruses. In this way, as well as by eventual deletion, captured functions may be lost as requirements diminish. Thus, the lineage leading to the cytomegaloviruses appears to have deleted the thymidine kinase gene in addition to losing the functions of the deoxyuridine triphosphatase and ribonucleotide reductase genes. Perhaps most impressively, smallpox (variola) virus has lost several functions in comparison with other poxviruses, many occurring by simple frame-shift mutations in what may be presumed to be recent evolutionary history. Indeed, the implication that virulence in smallpox virus may have emerged as a result of the loss, rather than acquisition, of genes is a stimulating one.

Hidden captives?

Captured cellular genes that retain their original function, albeit sometimes in modified form, are the most common type of viral gene thrown up by homology searches. What about other viral genes that lack cellular homologues, such as those encoding structural components of the virion? There are two main possibilities. Evidence for the first, generation of genes *de novo*, does exist for some genes that are small or significantly overlap other genes. A large leap is required, however, to accept that a significant number of such genes in the large DNA viruses arose by this means. It seems more attractive to suppose that these genes were also captured from the cellular repertoire and have undergone such extensive functional revamping that their origins are now undetectable. Also, this does not preclude additional superimposed events such as gene duplication and divergence. We should expect that possible cellular origins for these genes will be put to the test with accumulation of detailed information on viral protein structures. In this connection, it is instructive to note that we cannot be complacent about our understanding of the evolutionary rates of viral genes. Studies of human herpesvirus 8 have already thrown up an example of a gene undergoing positive selection – a situation which strongly favours mutations that change coding potential. Evolutionary modes that allow faster rates of change than those operating generally could have wider implications in the generation of viral genes.

We rightly marvel at the way in which viruses have exploited cellular genes in promoting their own survival and in the clues that homology searches give to how viruses have evolved. In trying to understand the most ancient viral origins, a large degree of simplification and a generous helping of speculation are required. Worthy as it is, the quest to trace modern viruses to their primary roots in a convincing way is likely to be arduous and long.

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Genomics, phylogenetics and epidemiology

Eddie C. Holmes

Comparison of the sequences of complete genomes of organisms may in future provide an opportunity to learn much more about why pathogens spread and cause disease and will allow us to unravel the crossed wires of evolutionary relationships.

If the history of genetics has taught us anything it is that each technological advance in data generation, from starch gel electrophoresis to PCR and automated DNA sequencing, has brought with it vast new amounts of information, and often new debates, about how genomes are organized and evolve, and how species are related. It is not difficult to predict that the first data revolution of the 21st century – the ability to sequence and compare the entire genomes of organisms – will likewise bring with it many new insights into the genetical history of life on earth.

Epidemiology is one science which will benefit from this flood of gene sequence data. Access to the complete genomes of microbial species will doubtless assist in the identification of the molecular factors which underpin fundamental biological properties like virulence and tropism, while on the host side genome data will allow us to determine the genetic basis of disease susceptibility and outcome. However, even though the availability of sequence data will no longer limit the type of questions asked, there are still challenges for those wishing to use it to understand the nature of infectious disease. First, it will be necessary to implement rational sampling protocols, controlling for factors such as age, sex, geographical location and disease classification, so that the sequence data we have are as informative as possible. Second, it will be necessary to develop a new suite of analytical tools which can effectively process such an abundance of information. It is likely that many of these tools will have their roots firmly planted in evolutionary biology – a field that provides a natural theoretical framework by which to understand why genomes are as they are.

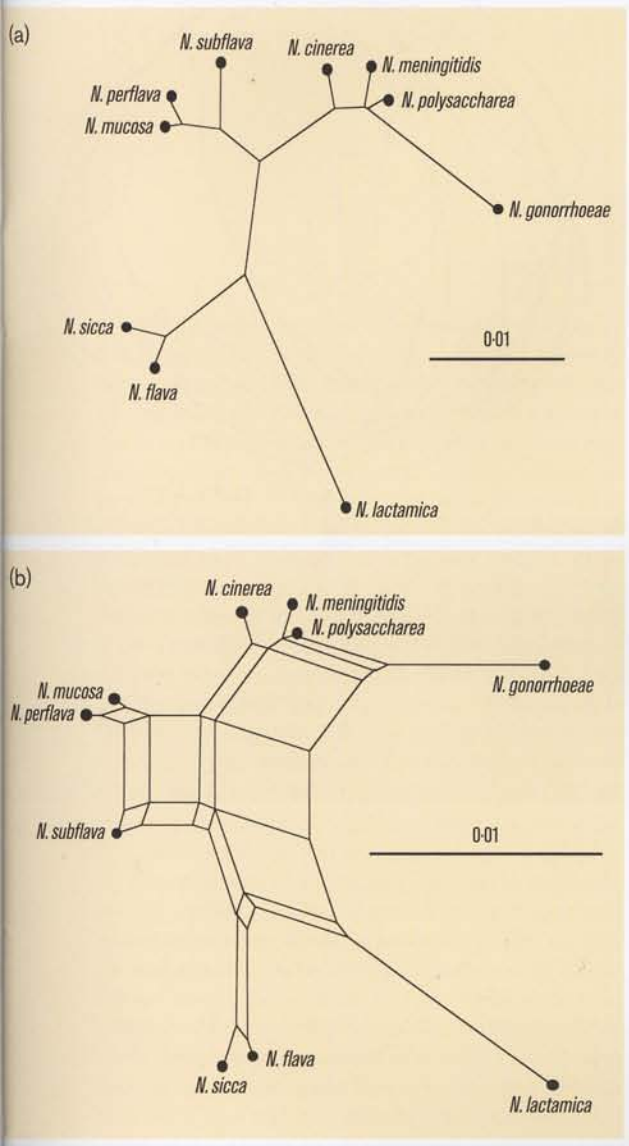
The phylogenetic vista

Perhaps the most useful tool in the evolutionist's kit is the phylogenetic tree. The growing sophistication of methods of phylogenetic analysis along with their ever wider application is one of the most significant developments in evolutionary biology. Since their first appearance in the early 1960s, gradual improvements have been made in the mathematical models used to describe sequence evolution, the proper starting point for any phylogenetic analysis. Not only can the models available today allow bases to change at rates specific to the data in hand, but methods are now so advanced as to allow changes in base composition along lineages and for different sites along a sequence to evolve at different rates, both of which can have profound effects on the trees constructed. Progress is also being made in allowing bases to evolve in a concerted fashion, as might be caused by protein or DNA/RNA secondary structure. Put together, these advances mean that the assumptions we make when we construct a phylogenetic tree are increasingly likely to mirror the evolutionary processes that produced the sequences in the first place. Furthermore, techniques of tree reconstruction are being developed which use gene position or gene order. Finally, we now know a good deal more about the circumstances under which we fail to obtain the correct tree, such as not having a representative sample of taxa, and so we can design our analyses accordingly. This being said, wildly differing rates of evolution or changes in base composition along lineages continue to cause problems in phylogenetic analysis and must always be considered as possible sources of error.

Once constructed, phylogenetic trees can be put to a variety of uses in epidemiology, including determining the source of particular epidemics, tracking their subsequent progress through populations and assessing whether certain strains are more often associated with outbreaks than others. More recently, phylogenetic methods, such as that of Nielsen & Yang (1998), have been developed which allow the identification of individual codons subject to positive selection. Such techniques obviously have enormous potential in the identification of those sites of utmost functional importance. Equally impressive is that phylogenetic trees can even provide an indication of rates of pathogen spread. The use of molecular phylogenies in this context stems from the realization that different demographic histories (i.e. rates of population growth or decline) alter the rates at which lineages appear on the tree. As a simple rule, trees reconstructed from a (small) sample of lineages from a population which has maintained a constant size through time will tend to have more branching (= coalescent) events towards the tips than at the root. As the rate of population growth increases, branching events move from the tips towards the root, from which dynamic it is possible to estimate approximate growth rates. It is therefore possible to measure the growth characteristics of epidemics simply by studying the branching structure of phylogenetic trees. As a case in point, application of this method to HIV-1 sequence data revealed different rates of population growth for viral subtypes A and B, suggesting that there was an initial rapid spread of subtype B viruses through high risk populations in Europe and North America. It is clear that as theory develops further, so we will be able to infer more complex epidemiological histories simply by examining gene sequences.

Trees or networks?

Although we can construct phylogenetic trees with more accuracy than ever before, and can ask more far-reaching epidemiological questions, this in itself does not necessarily mean that we are putting together a more accurate picture of evolutionary relationships. The limitation of most phylogenetic analyses is that a tree is merely a hypothesis of how sequences and species might be related to each other – albeit generally a very good one – and that there are other, more complex, ways



LEFT
Fig. 1. (a) Unrooted neighbour-joining tree of 16S rRNA sequences (1355 bp) from ten species of *Neisseria*. (b) Network representation of the same data drawn using the method of split decomposition, which shows all the phylogenetic pathways (i.e. the splits) linking sequences rather than only those that fit into a single tree. More information concerning these data and the analytical methods used can be found in Smith *et al.* (1999).

in which organisms can be connected. For example, if a sequence has undergone recombination in its evolutionary history, a process which is common within and among many microbial species, then it may be more realistic to depict their evolutionary relationships as an intricate 'network' diagram in which sequences have multiple ancestors, rather than as the normal bifurcating tree with a single ancestral sequence at each node. It is equally clear that recombination in the form of lateral gene transfer has been widespread across very great evolutionary distances, a process which will greatly complicate our desire to reconstruct the tree of all cellular life and to classify organisms in a simple hierarchical manner.

Deciding whether evolutionary patterns are better represented as trees or networks is not only a taxonomic nicety, but it also has profound implications for understanding evolutionary mechanisms and predicting future trends. For example, loci exhibiting high rates of recombination, and which form network structures, will have a greater capacity to generate genetic variation and hence have more adaptive potential than those in which mutation is the only fuel for diversity, and so evolve in a tree-like manner. Such accelerated evolutionary change is of special importance in antigen-encoding genes or those that determine drug or vaccine resistance. A key phylogenetic question for the future is, therefore, which genes evolve in a simple tree-like manner and which show more complex structures, as this provides a simple window on evolutionary mechanism.

Despite the evident importance of networked evolution, most methods of phylogenetic analysis will draw a tree regardless of the underlying evolutionary process and in doing so will misrepresent evolutionary history. As an example, consider the relationships between various species of *Neisseria* bacteria reconstructed using the 16S rRNA gene, a gene often used in the phylogenetic analysis of microbial species. Although a simple neighbour-joining tree of ten of these species appears to be a reasonable interpretation of their phylogenetic relationships (Fig. 1a), it ignores the fact that many interspecific recombination events have occurred. In these circumstances a network structure is a much more realistic reconstruction of their evolutionary history (Fig. 1b). It is perhaps ironic that as gene sequence data accumulates and phylogenetic trees become ever more common and powerful analytical tools, there is a growing realization that these trees are not always the best representation of evolutionary history.

The ability to sequence and compare the complete genomes of organisms promises much to many areas of biological science. For evolutionary biologists these data will allow us to unravel the crossed wires of evolutionary relationships, while for epidemiologists they provide a major opportunity to learn why pathogens spread and cause disease. The challenge for bioinformatics, now a key component in both disciplines, is not only to devise more efficient computer programs to analyse the abundance of gene sequence data, but also to infer more complex patterns of evolutionary relationships, and hence mechanisms, from these sequences.

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Further reading

Nielsen, R. & Yang, Z. (1998). Likelihood models for detecting positively selected amino acid sites and applications to the HIV-1 envelope gene. *Genetics* 148, 929–936.

Pybus, O.G., Holmes, E.C. & Harvey P.H. (1999). The mid-depth method and HIV-1: a practical approach to testing hypotheses of viral epidemic history. *Mol Biol Evol* 16, 953–959.

Smith, N.H., Holmes, E.C., Donovan, G.M., Carpenter, G.A. & Spratt, B.G. (1999). Networks and groups within the genus *Neisseria*: analysis of *argF*, *recA*, rho and 16S rRNA sequences from human *Neisseria* species. *Mol Biol Evol* 16, 773–783.

Genomic landscapes

Jean R. Lobry

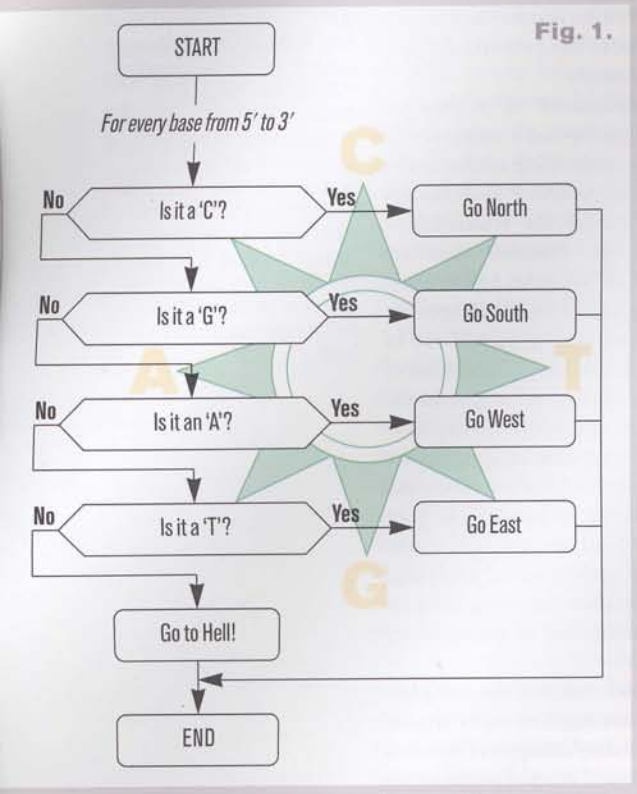


Fig. 1.

DNA walks

The recent availability of complete microbial genome sequences to the scientific community has opened the door to undoubtedly useful new bioinformatic approaches such as playing DNA music or drawing DNA walks. Since I hate noise, I will focus on DNA walks. To obtain a DNA walk all you need is a DNA sequence, a sheet of paper and a pencil to draw with using the instructions given in the chart on the left (Fig. 1).

Read the DNA sequence and walk into the plane according to the four directions defined by the four different bases. For a complete genome, this repetitive task could be extremely tedious but fortunately a computer is not easily bored. Now look at the output obtained with the 3,573,470 bases of the complete genome of *Synechocystis* PCC 6803, a cyanobacterium (Fig. 2).

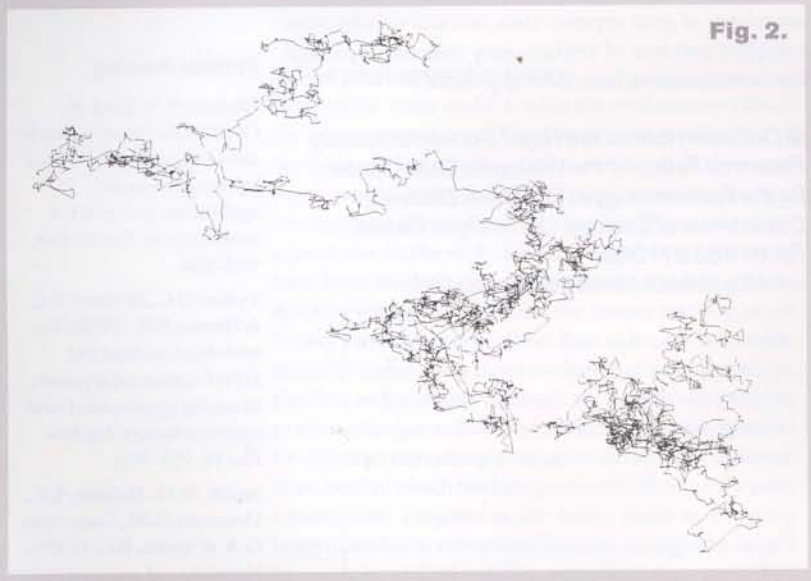


Fig. 2.

Here we have a simple graphical display corresponding to the complete genome sequence of this bacterium. What does it suggest to you? Yes, I know, a 3-year-old child could do that (see Fig. 3!!).

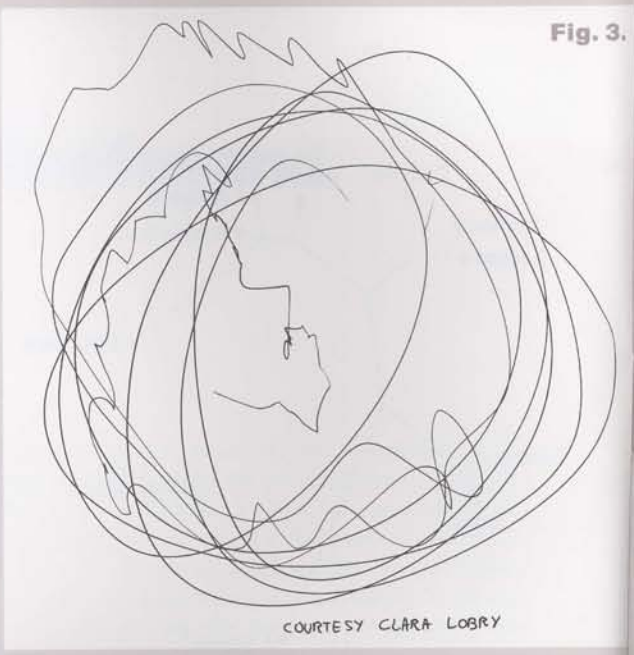


Fig. 3.

Hum. I agree that for *Synechocystis* it does look like nothing. But now look at *Borrelia burgdorferi*, a spirochaete (Fig. 4). The genome of this species is so incredible that the first time I analysed it I wondered if there were bugs in my program. Since then, the genome of *B. burgdorferi* has been analysed independently by other people and I am sure that this picture is not an artefact.

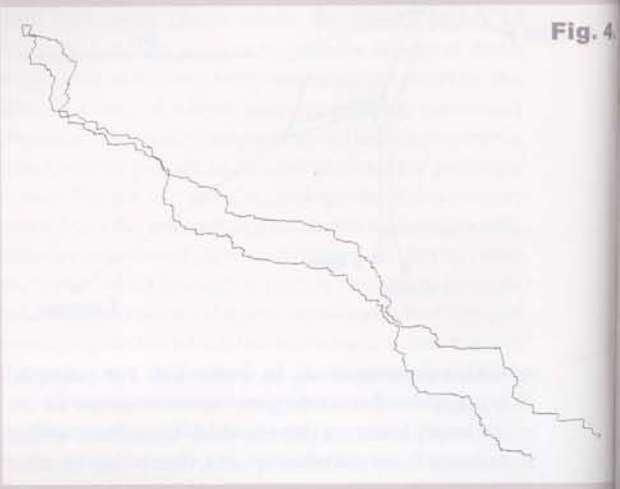


Fig. 4.

The pattern is much more regular than the previous random coils. Now if you plot, say, the 'y' co-ordinate of the walk, corresponding to the 'C-G' axis, against the map position on the chromosome you obtain the graph shown in Fig. 5.

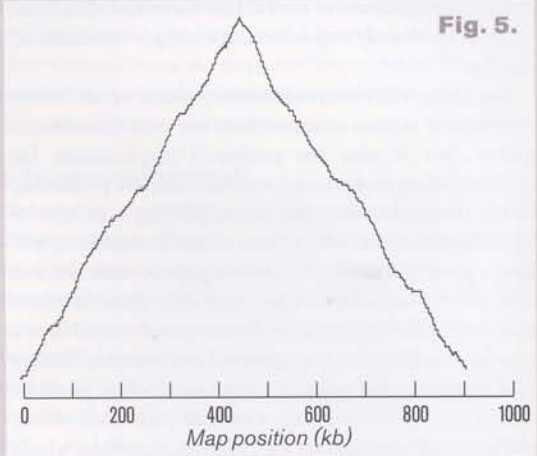
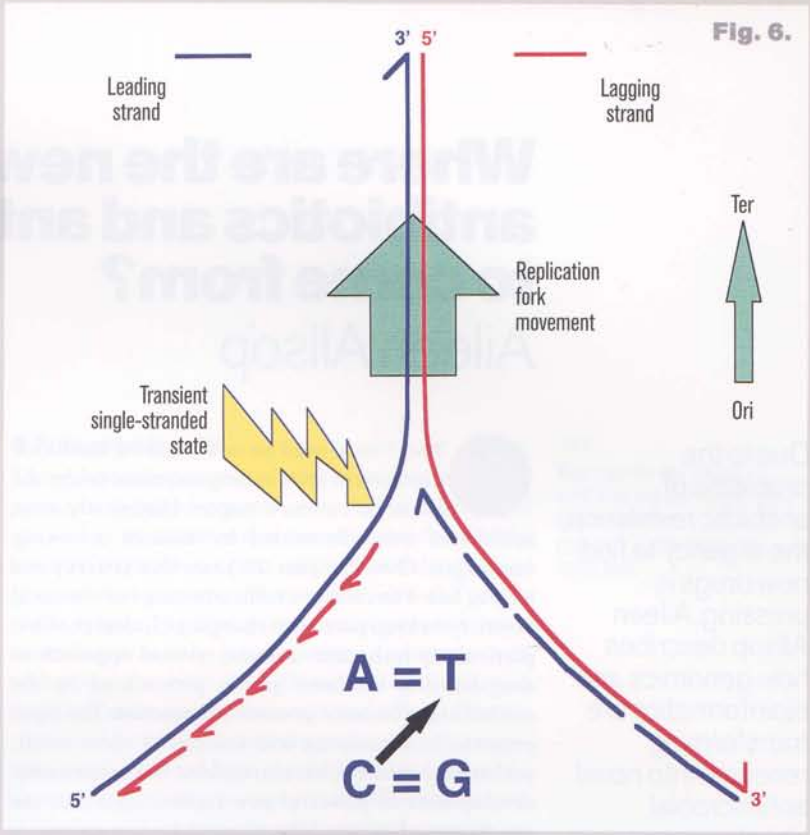


Fig. 5.



Now do you get it? This is a mountain – a *genome landscape*! The title of the article becomes comprehensible. But what is the meaning of this mountain? Simply that there are systematic statistical biases for the base composition along the chromosome. Travelling from 5′ to 3′ you start to climb the mountain, meaning that on average there is an excess of C over G in the sequence. Then when you start to go down the mountain it means exactly the opposite, i.e. there is an excess of G over C in the sequence. As you can see, the mountain slopes are approximately the same on both sides, meaning that these biases are symmetrical: their intensity is the same, the sign is just switched at the top of the mountain.

Climbing mountains

Do you know what is at the top of this mountain? It is the origin of replication of the *B. burgdorferi* chromosome that, incidentally, has just been experimentally mapped. As a consequence, when you are climbing the mountain you are reading the lagging strand for replication and when you are going down the mountain you are reading the leading strand for replication. What is usually found, but not always if you remember *Synechocystis*, is that the leading strand is enriched in keto (G or T) bases and that the lagging strand is enriched in amino (A or C) bases. Interestingly, these biases have been reported for both eubacteria and archaea, mitochondria, chloroplasts, viruses and plasmids, but not for eukaryotes up to now. In *B. burgdorferi* the biases are so important that they affect the amino acid content of proteins and you can guess if a protein was encoded on the leading or the lagging strand solely from its amino acid content.

The term 'chirochore' was coined to describe fragments of the genome corresponding to a mountainside, that is a DNA fragment more or less homogeneous for the base composition biases. This is a purely descriptive term without reference to any mechanism, reminiscent of 'isochore' for the description of DNA fragments with a homogeneous G+C content in some vertebrate chromosomes. On the other hand, the term 'replichore' was introduced to designate the two oppositely replicated halves of the chromosome between the origin and the terminus in bacteria. The good thing is that chirochore and replichore boundaries are the same in bacteria: the origins of replication are found at the top of the mountains while the termini are found at the bottom of the lowlands. This strongly suggests that these kinds of genome landscapes have something to do with replication.

Genomic tectonics

A simple model to explain the universality of the phenomenon is based on the spontaneous deamination of cytosines that induce C→T mutations. The rate of this deamination is highly increased in single-stranded DNA, probably because of greater accessibility to the solvent in this state than in the double-stranded state. During replication the lagging strand is continuously protected by the newly synthesized leading strand, but the leading strand has to maintain a transient single-stranded state while waiting for the next Okazaki fragment to be long enough to restore the double-stranded state (see Fig. 6).

This fundamental asymmetry of replication may explain the universality of the observed systematic biases in base composition; these are at least compatible with the hypothesis. The protection against cytosine deamination may differ between species and explain the variability in intensity of biases.

The cytosine deamination theory is nice but it is just a theory. The fundamental limit of bioinformatics is that without experimental data you can discuss *in silico* results endlessly and fruitlessly. I would be very curious to know the minimum inhibitory concentration (MIC) of chemicals such as bisulphite, which catalyses the deamination of cytosine, for bacteria in which compositional biases are important (for instance *B. burgdorferi*, *Treponema pallidum*, *Neisseria meningitidis*). These compounds may not only inhibit replication but also transcription because during transcription a transient single-stranded DNA state is necessary too. It would also be interesting to determine toxicological information for eukaryotic cells.

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Further reading

A good introduction to DNA music and courses on bioinformatics and DNA correlations, among other subjects, is Wentian Li's home page at **http://linkage.rockefeller.edu/wli/**

More about DNA walks, their transformations and analysis, is available on the smORFland home page at **http://smorfland.microb.uni.wroc.pl/**

The story of the *Borrelia burgdorferi* replication origin can be found in:
Picardeau, M., Lobry, J.R. & Hinnebusch, B.J. (1999). Physical mapping of an origin of bidirectional replication at the centre of the *Borrelia burgdorferi* linear chromosome. *Mol Microbiol* 32, 437–445.

The underlying mechanisms that may explain genomic landscapes were recently reviewed in:
Frank, A. C. & Lobry, J. R. (1999). Asymmetric substitution patterns: a review of possible underlying mutational or selective mechanisms. *Gene* 238, 65–77.

Where are the new classes of antibiotics and anti-fungals going to come from?

Aileen Allsop

Due to the problems of antibiotic resistance, the urgency to find new drugs is pressing. Aileen Allsop describes how genomics and bioinformatics are transforming research into novel antimicrobial agents.

The clinical need for new classes of antibiotic continues to grow as drug resistance erodes the efficacy of current therapies. Historically, most antibiotics were discovered by random screening campaigns. Over the past 20 years this strategy has largely failed to deliver a sufficient range of chemical diversity to keep pace with changing clinical profiles, particularly resistance. A more rational approach to drug-hunting has been greatly potentiated by the availability of bacterial genomic information. The rapid progress in sequencing and analysis of these small, prokaryotic genomes has also enabled the concomitant development of powerful new technologies that are rapidly extending our ability to search for new agents.

Approaches to drug hunting

In the past few years pharmaceutical research has concentrated on two basic approaches in searching for novel antibacterial and anti-fungal compounds, either target-based, semi-rational programmes or anti-microbial screening. Both of these have advantages and shortcomings as shown in Tables 1 and 2.

On balance the overall advantages of the target-based strategies are obvious and many companies have now abandoned random screening of either chemical banks or natural products. An ideal target should be different, essential to microbial cell survival, highly conserved in a clinically relevant spectrum of species and absent or radically different in man. Inhibition of this activity could therefore cure the infection by killing the potential range of bugs involved without damaging the patient and activity should not be restricted by existing resistance mechanisms. Furthermore, the ideal target should be easy to assay, and therefore screen, and be suitable for rapid structural analysis. None of this, of course, is as easy as it seems! Searching electronic databases can provide a quick profile of the current state of knowledge around a specific gene. Bioinformatics has had the greatest impact, however, in genomic analysis, highlighting potential targets with interesting properties: for example a number of companies have built comparative genomic platforms which are effectively capable of simultaneously comparing entire genomes of a whole range of pathogenic species and producing a rank order of conserved genes. This can now be achieved for a whole variety of clinically relevant spectra, including organisms as diverse as *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Mycoplasma pneumoniae*. Dissimilarity to the human genome can also be built into the analysis, resulting in a list of targets with potential selectivity over man and a useful spectrum. Whether the target is essential is the next question to answer. Simplistically, gene knock-outs can easily provide this evidence; however, in reality it is very easy to be misled. A total loss of function (as created in a full gene knock-out) is an unlikely outcome from biochemical inhibition by a compound in most cases. Our work at AstraZeneca has demonstrated a surprising number of genes which by definition are essential to microbial cell survival, but where even trace expression levels can rescue viability.

Table 1. Random-screening-based drug hunting

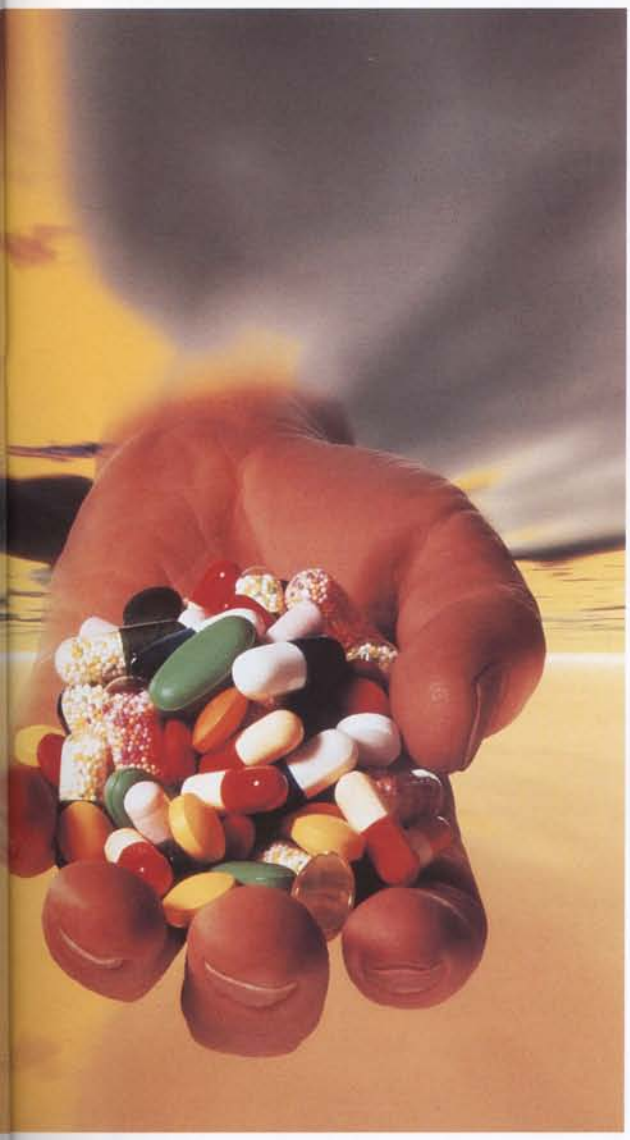
Advantages	
	■ Selection for compound series which penetrate cells
	■ Inhibitor → antimicrobial already present
	■ Reproducible
Disadvantages	
	■ Most active compounds are toxic and non-specific
	■ No rational basis for compound optimization
	■ Spectrum unpredictable
	■ Mixed mechanisms of action common

Table 2. Target-based drug hunting

Advantages	
	■ More sensitive – will pick up weak inhibitors and compounds which do not penetrate (these can be the starting point for a chemical programme)
	■ Easy screening – enzyme inhibitors
	■ Different approach (rational basis) and conventional screening is not highlighting many new agents
	■ Ability to drive the search for novel compounds into new areas of biology
	■ Ability to do rational drug design
Disadvantages	
	■ Need to turn *in vitro* enzyme inhibitor into antibacterial drug – not easy
	■ Genetic validation of targets can be misleading

Functional genomics

Having selected a target which theoretically can be used to identify a compound of interest, the next step is to transform theory into practice and design suitable screens. Happily, there are many suitable targets with established biochemistry which have not yet been exploited in the clinic. Under these circumstances assay development can be a trivial exercise and screening can progress rapidly. However, there are some extremely attractive targets which are poorly understood in terms of function and biochemistry. Functional genomics is an umbrella which brings together both bioinformatic, genomic, genetic and biochemical analysis to understand and investigate genes of this type. The power of linking information and approaches in this way is perfectly illustrated by the Yeast Functional Data Base;



LEFT:
Where are the new classes of antibiotics and anti-fungals going to come from?
COURTESY JOSEPH DRIVAS/THE IMAGE BANK

reference to this source can provide a starting point for investigation if not real evidence of analogous proteins. In addition, many researchers have designed whole-cell screens which respond to inhibition of specific targets, without any prior understanding of biochemistry or function.

New applications of genomics

This is the point at which, until recently, the benefits of a genomic-based approach stopped. Conventional drug-hunting involves high throughput screening of compound banks, analysis of hits and rapid expansion of active chemical series to establish true lead compounds with antimicrobial activity. Alternatively, rational design using structural information for guidance can lead to the same outcome. Lead optimization then methodically selects for improvements in drug-associated properties such as minimum inhibitory concentration (MIC), spectrum, bioavailablity and pharmacokinetics, until finally suitable development candidates are identified. Even with state-of-the-art chemical technologies, such as combinatorial chemistry or multiple parallel synthesis, chemical diversity cannot always deliver the desired compound profile and failure is a constant risk throughout this process. Many companies have used genomics to select interesting new targets; screening has revealed inhibitors and in some cases compounds with significant antimicrobial activity. However, there are no examples of compounds in development which have come from these strategies, but it is still early days.

Future potential

The technologies associated with microbial genomics, particularly bioinformatics, have radically changed our ability to follow target-based approaches. Sadly, however, targets do not treat infections and the chemical properties of a compound may not fulfil the profile of the target. The next generation of genomic-based technologies is only just beginning to impact upon addressing the risks of such strategies. Expression profiling (microarray), proteomics and mutant libraries combined have established the technology to investigate, confirm, or establish the mechanism of action of a compound, providing an important link between targets of interest and compounds with attractive properties. These technologies extend our capabilities further in the area of functional genomics and also provide new tools for the latter stages of drug-hunting, but the greatest impact could be in facilitating the transformation of antimicrobial screening campaigns into rational genomics-based drug-hunting programmes. Other tools are also emerging which could improve the quality of our decision-making, for example structural genomics will deliver an improved capability to judge the similarity of microbial target enzymes against human counterparts. An ideal technology platform would allow for the combined advantages of both compound and target-based screening. There is every reason to be optimistic that this will be possible in the very near future.

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Horizontal transfer of genes in bacteria

Paul H. Roy

Horizontal transfer of genes in bacteria has been studied for several years, especially with regard to extrachromosomal elements. Genomic sequencing is now providing increasing evidence for widespread exchange of chromosomal genes. I will attempt to provide a brief overview of the mechanisms of genetic exchange and of mobile DNA, and then summarize how genomic data can be searched for evidence of horizontal transfer.

Mechanisms of genetic exchange

Conjugation. Conjugation has been well studied, especially in *Escherichia coli* and *Pseudomonas aeruginosa*. In these species, sex factor (F and FP) plasmids can become integrated into the chromosome by homologous recombination between an insertion sequence (IS) on the plasmid and a homologous IS on the chromosome. Subsequent pilus synthesis and initiation of single-strand displacement replication then causes the transfer of half of the F plasmid followed by a large segment of chromosomal DNA, via the pilus, into a recipient cell. There, the second strand is synthesized and the acquired DNA is incorporated by homologous recombination. Alternatively, the F factor can be aberrantly excised to form an F′ factor (a large circular plasmid containing many chromosomal genes) which can be transferred by the same mechanism. Because of the host range of the F plasmid, transfer between *E. coli* and *Salmonella* can occur. Amongst Gram-positive organisms, streptococci are the best studied and contain both conjugative plasmids and conjugative transposons (see below).

Transformation. This mechanism, while not ubiquitous, has been well studied in both Gram-positive (*Streptococcus pneumoniae* and *Bacillus subtilis*) and Gram-negative (*Haemophilus influenzae* and *Neisseria gonorrhoeae*) bacteria. Several other species are known to have natural transformation systems, among them *Acinetobacter* (where transformation may be the major mechanism of dissemination of antibiotic resistance in this species) and the cyanobacterium *Synechocystis*. The completion of the genomic sequences of *B. subtilis* and *H. influenzae* and the identification of their competence genes makes it possible to search for homologues in other species.

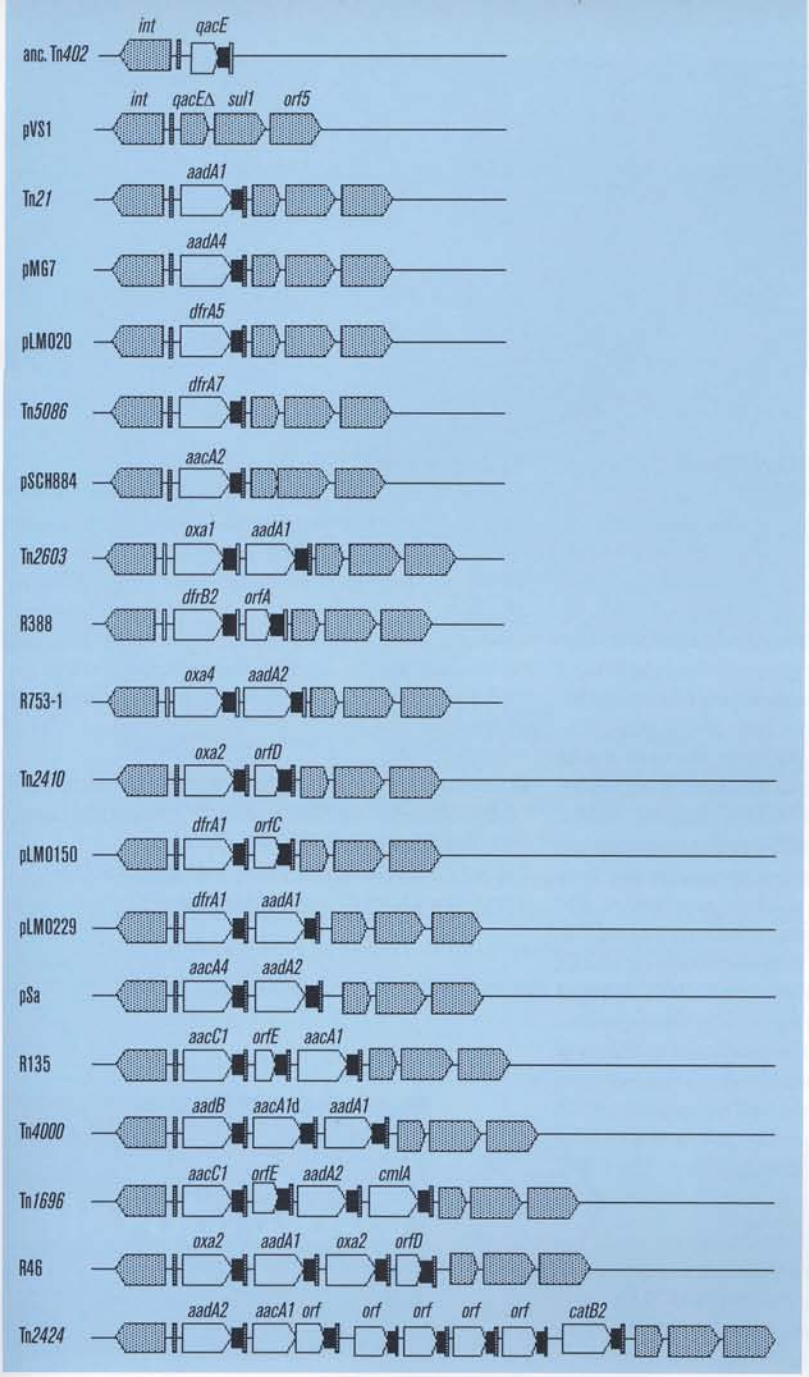
Transduction. Two types of transduction exist: specialized (by aberrant excision of a lysogenic phage, incorporating genes adjacent to the phage attachment site) and generalized (by erroneous encapsidation of chromosomal DNA in lieu of linear phage concatameric DNA produced by rolling circle replication). The specificity is restrained by the phage host range; this is probably not a major mechanism of interspecies transfer.

Vehicles for genetic exchange

Plasmids. Plasmids have been best studied in *E. coli* and *P. aeruginosa*. Early on they were divided into F (sex factor) and R (resistance) plasmids. Later, many R plasmids were found to encode F-like replication and/or transfer genes. Conjugative R plasmids are responsible for most of the dissemination of antibiotic resistance genes. One of the best studied is R100, which contains F-like transfer genes but different replication genes. Within R100 there is a transposon, Tn*10*, encoding tetracycline resistance, and another transposon, Tn*21*, encoding mercury resistance, itself within a Tn*9*-like transposon encoding chloramphenicol resistance. Within Tn*21* there is an integron encoding streptomycin and sulphonamide resistance. While the aforementioned are typically extrachromosomal genes, plasmids can also carry chromosomal genes. A good example is the class C chromosomal β-lactamases, whose genes are increasingly found on plasmids. As mentioned above, F plasmids can transfer large blocks of chromosomal genes.

Transposons. Transposons, or 'jumping genes' are responsible for the dissemination of several antibiotic and heavy metal resistance genes, as well as degradative genes and even the lactose operon (the latter with the consequence that clinical microbiologists can no longer ignore Lac^+ enterobacteria!). Perhaps the best-known example is Tn*3*, which contains two genes for its own transposition and the TEM-1 β-lactamase gene. Tn*3* has spread among *Enterobacteriaceae* on plasmids of several incompatibility groups (which correspond to replication functions and thus to host ranges). But perhaps the best example of horizontal transfer by transposons is the arrival of Tn*3* in *Haemophilus* and *Neisseria* in the mid-1970s. Although not all the pieces of the puzzle can be retraced, the most likely scenario would involve the transfer, by conjugation or transformation, of an *E. coli* plasmid carrying Tn*3* into *Haemophilus ducreyi* (the agent of soft chancre). The plasmid would not have been able to replicate (*E. coli* plasmids are unknown in *Haemophilus*) but before it was degraded, its Tn*3* 'hopped' onto a native plasmid. The *H. ducreyi* plasmids are the 'smoking gun' since they contain all of Tn*3*. A 'streamlined' version, having lost the transposase gene (no longer necessary since the plasmids are spread among *Haemophilus* and *Neisseria* by transformation), is found not only in *H. ducreyi* but also in *Haemophilus parainfluenzae* and *N. gonorrhoeae*, where it caused the emergence of the well known penicillinase-producing *N. gonorrhoeae* (PPNG). Surprisingly, the TEM gene in these organisms has not produced the wide variety of extended-spectrum TEM β-lactamases found in *Enterobacteriaceae* despite the widespread use of ceftriaxone to treat PPNG – does *N. gonorrhoeae* have a very faithful DNA polymerase?

Complex transposons, such as Tn*5*, are composed of a central section, typically containing one or more antibiotic resistance genes, flanked by inverted or direct repeats of ISs. These transposons are probably formed by



LEFT:
Fig. 1. Some representative integrons. Genes in the 5′ (*int*) and 3′ (*qacE*Δ, *sul1*, and *orf5*) conserved segments are represented by shaded boxes. The GTTRRRY core sites are represented by vertical bars. '59-base elements', which terminate in core sites, are represented as black rectangles. The first line (anc. Tn*402*) represents a hypothetical ancestor of Tn*402*, in which the *qacE* cassette is complete. In all other integrons shown, *qacE* is truncated, two of the four transposition genes lost, and *sul1* and *orf5* non-specifically inserted. Transposition genes are not shown since their distance from *orf5* varies between the elements.

transposition of ISs to either side of a region of DNA. Indeed, any region of chromosomal DNA which becomes flanked by copies of the same IS can potentially become a transposon. This should be looked for in sequence analysis of chromosomal DNA near putative IS elements.

Conjugative transposons are found in Gram-positive bacteria and encode the mechanism, yet to be described in detail, for their own transfer. They encode an integrase and an excisase related to those of temperate phages. Among these are Tn*916*, encoding tetracycline resistance, Tn*1545*, encoding erythromycin resistance, and Tn*1547*, encoding one type of vancomycin resistance (another is carried on Tn*1546*, a Tn*3*-type transposon).

Integrons. Much of the dissemination of antibiotic resistance in Gram-negative bacteria is due to integrons. Evidence for their existence was hinted at by restriction maps and heteroduplexes, demonstrated by electron microscopy, which pointed to gene-sized differences among related plasmids and transposons. Sequencing confirmed that a mechanism of site-specific recombination, mediated by an integrase, was at work. Integrons are elements in which structural genes, each linked to a palindromic '59-base element' (*attC* site), are assembled as cassettes into operons by insertion at an attachment (*attI*) site. A strong promoter adjacent to the *attI* site makes integrons a sort of natural expression vector. In class 1 integrons, the most frequent kind, the integrase and *attI* site (from a cryptic phage in chromosomal DNA?) became associated with a Tn*5053*-like transposon, and a few have retained this association, e.g. Tn*402* of plasmid R751. Similarly, class 2 integrons became associated with an ancestral transposon to form Tn*7*, whose integron carries its resistance genes. Most elements carrying class 1 integrons are descended from an element which acquired sulfonamide resistance (in the 1930s?), but in turn lost two of the four transposition genes. However, one of these was able to regain mobility by inserting into a mercury resistance transposon, Tn*2613*, to form Tn*21*. Many different cassette arrangements are found in Tn*21*-like transposons.

Although no direct chromosomal ancestor of class 1 or 2 integrons has yet been found, genomic sequencing has revealed several new classes of integrons, indicating that they are ancient mechanisms of gene exchange which have only recently been co-opted for dissemination of antibiotic resistance. In *Vibrio cholerae* there is a 'super-integron' in which over 150 cassettes (mostly unidentified genes), each with a palindromic 'VCR repeat' (a variant *attC* site) are aligned in a row next to an integrase gene. Other classes of integrons exist in *Xanthomonas campestris* pv. *badrii*, *Shewanella putrefaciens*, and in *Nitrosomonas europaea*. The *attC* sites in their cassettes are much more similar to the '59-base elements' of class 1 integrons than are VCR repeats. The integrases of the various classes, however, all show 45–60% amino acid identity between themselves.

The arrangement of some representative integrons is shown in Fig. 1.

Further reading

Jain, R., Rivera, M.C. & Lake, J.A. (1999). Horizontal gene transfer among genomes: the complexity hypothesis. *Proc Natl Acad Sci USA* 96, 3801–3806.

Recchia, G.D. & Hall, R.M. (1995). Gene cassettes: a new class of mobile element. *Microbiology* 141, 3015–3027.

Roy, P.H. (1999). Transposons and integrons: Natural genetic engineering of antibiotic resistance. *Can J Infect Dis* 10, suppl. C, 4C–8C.

Evidence from sequence data for horizontally transferred genes

G+C anomalies. Even before the sequencing of complete genomes, it was possible to identify certain chromosomal genes as having an origin different from that of other genes from the same organism. Sometimes this can be done when relatively few genes have been sequenced. An example is the gene encoding the BRO-1 β-lactamase of *Moraxella catarrhalis* (which causes otitis media; this species went from <10 to >80 % penicillin-resistant in a few years). The *bro1* gene shows an abrupt shift in G+C content relative to its flanking sequences. This gene, apparently of Gram-positive origin, substituted its ~1000 bp for a 75-bp, mostly intergenic, region found in penicillin-sensitive strains, and in so doing became the third gene of a four-gene operon. The surrounding ORFs show strong similarity to *gatCAB*, encoding glutamyl-tRNA^{Gln} amidotransferase (AdT), usually associated with Gram-positive bacteria. It might appear at first that the whole region is of Gram-positive origin. However, the recently completed genomes of *P. aeruginosa* and *Neisseria meningitidis*, Gram-negative bacteria in which AdT is present and asparaginyl-tRNA synthetase is absent, point to another role for this enzyme – asparaginyl-tRNA^{Asn} amidotransferase. The ORFs would thus be essential genes native to *M. catarrhalis*.

Codon usage. Not all G+C anomalies are related to horizontal transfer; the two anomalous regions in the *H. influenzae* genome correspond to the rRNA operon and to a cryptic phage. When as few as 10–20 genes have been sequenced from an organism, it is possible to construct a codon usage table, which reflects G+C content and also the relative abundance of tRNAs in an organism. Genes, especially those for highly expressed proteins, tend to conform to the codon usage patterns. Exceptions can indicate recent acquisition by horizontal transfer. Examples are the PAK and PAO pilin genes of *P. aeruginosa*. Their anomalous codon usage indicates that their genes have not evolved over a long period in these species.

Phylogenetic tree anomalies. A high degree of similarity of a gene with that of a genetically distant organism may be an indication of horizontal transfer. Similarly, phylogenetic trees for genes common to several sequenced genomes may show anomalies when compared to the rRNA tree. This is less common with informational genes (e.g. those involved with transcription and translation) than with other genes (there are some interesting exceptions, e.g. glutaminyl-tRNA synthetase genes). The rates of evolution for the two groups are similar and the anomalies in phylogenetic trees made with single genes other than informational genes provides evidence for continual events of horizontal transfer during the evolution of prokaryotes.

Conclusions

Antibiotic use creates a heavy selective pressure which permits us to observe, practically in real time, the evolution of bacteria using pre-existing mechanisms which, before the antibiotic era, were used for exchange of other sorts of genes. This rapid evolution has made extensive use of extrachromosomal elements, but evidence for longer-term exchange at the level of the chromosome can be detected by genomic sequence analysis.

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Edward Jenner and vaccination in context: Lady Mary got there first

Peter Balfe

Peter Balfe reviews a new book by Isobel Grundy, *Lady Mary Wortley Montagu, Comet of the Enlightenment*, in which it is suggested that Jenner's reputation as the pioneer of vaccination may be somewhat undeserved.

It is always refreshing to find out something you didn't know, or thought you knew and subsequently find to be false. We are all familiar with the school text version of Edward Jenner's great bravery in daring to challenge the recently vaccinated James Phipps with smallpox and of how he survived it. Now, from a new biography of Lady Mary Wortley Montagu by Isobel Grundy (1), it becomes apparent that the bravado invested in Jenner's experiment is somewhat undeserved.

In her biography of this 18th century poet, and occasional medical pioneer, Isobel Grundy shows us the life of the woman who generated a widespread acceptance of 'variolation' as an approach to smallpox prevention in 18th century Britain. Variolation involved placing a small quantity of smallpox in a small scratch or incision on the surface of the skin. The incision was then bound up to prevent transmission and the subject isolated from the world until the very mild attack of smallpox which ensued had completely subsided. Lady Mary, who survived smallpox in 1715, met up with this practice whilst in Turkey (where her husband was the British ambassador); she had both of her children treated in this way.

When she returned from Turkey in 1721 Lady Mary set about publicizing the method (2). In her favour were the facts that she was of an impeccable aristocratic lineage (the Pierrepoints and Montagus from whom she descended were both major forces in English society) and that she could write well of her experiences and expect to be listened to. Her credentials as a poetess were already well established and at the time of her return from Turkey she was widely regarded as the greatest female intellect of her age. However, at a time when women in general, and great ladies in particular, were expected only to fulfil completely decorative functions, she placed a great strain on society by her effrontery in being openly better read and better (self) educated than most of the men she met. As a result she became the target of massive misogynist prejudice and was derided as an aberration. At the same time, a widely publicized feud with Alexander Pope damaged her literary reputation. As a final insult, in those publications which were inclined to accept the practice she advocated, her husband was often given all the credit. Irrespective of their effects on Lady Mary herself, as a result of her activities variolation became commonplace amongst the aristocracy; for example, a big boost to popularity was received when Caroline, Princess of Wales, had two of the royal children variolated.

BELOW:
Lady Mary Wortley Montagu with her son and attendants. Artist: attributed to Vanmour, Jean Baptiste (1671–1737). Date: c. 1717.
COURTESY OF THE NATIONAL PORTRAIT GALLERY, LONDON

The practice became one which was fiercely debated throughout the 17th century. The Rev. Edmund Massey, who had previously preached on the benefits of the plague as a judgement of God, attacked the practice as evading divine punishment. Furthermore, several deaths from variolation occurred, mostly as a result of medical experts 'improving' on the heathen Turkish model, by pushing more and more smallpox into larger and larger wounds and combining this treatment with other beneficial practices such as bloodletting. A controversial literature of claims and counterclaims built up round the field, though opinion was united on the subsequent immunity to

smallpox of those who survived variolation.

It is hence inconceivable that Edward Jenner was not educated in this during his medical training. In this light his inoculation of James Phipps with Vaccinia, followed by inoculation with Variola, seems less of a scientific leap in the dark. Jenner's prior knowledge of Lady Mary's work makes the step he took seem both smaller and more scientifically justified. Jenner would have known precisely how little risk he was placing his patient under, and that the 'endpoint' for his experiment if it had failed was probably not full-blown smallpox, but the mild fever and rash associated with successful variolation.

Lady Mary herself eventually found the pressure of dual notoriety intolerable. She left the country in 1739 in lovelorn pursuit of a young gentleman half her age. She fell out of sight for 20 years, living at various times in Venice, Southern France and the Po valley. Although she never pursued publication of her poems, several of her works found themselves in anthologies of contemporary poetry (without her permission). She eventually returned to Britain in 1762 after the death of her husband. She was instantly famous all over again, partly because by then her daughter was the wife of the Earl of Bute, the Prime Minister. It is arguable as to which of her dual legacies, in poetry and medicine, was the more important, but reading this account of her life makes it clear that this unusual, opinionated and influential woman had a major impact on her world.

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Website: http://www.ucl.ac.uk/windeyer-institute

Further reading

1. Isobel Grundy (1999). *Lady Mary Wortley Montagu, Comet of the Enlightenment*. Oxford University Press (£30.00, pp. 680, ISBN 0-19-811289-0).

2. Anthony Henricy, Aix (1796). *Letters of the Right Honourable Lady Mary Wortley Montagu: Written During Her Travels in Europe, Asia and Africa*, Vol. 1.

MicroShorts

Save British Science Society

The SGM is pleased to support SBS, an organization which campaigns effectively to promote the cultural and economic importance of science, engineering and technology in the UK. SBS communicates with Government, industry and the public. Its activities focus on four main areas:

- Science and engineering base
- Science and the economy
- Science and education
- Science in society

The latest *Annual Review of Activities* reports many changes and successes. The organization moved to offices in London and a new post of Director was established to run the Society. A Labour government came into power with consequent changes in science policy and ministers. Representatives from SBS have been in discussions about the science base with the new Prime Minister and other relevant officials; they have pressed for many improvements to science policy and funding and submitted evidence to consultation documents. In the past year SBS has published numerous reports and briefings and obtained significant media coverage on important issues.

SGM is one of 20 scientific societies who are members of Save British Science, but there are 1,500 individual members. For details of membership, telephone **0171 504 4995** or e-mail **sbs@dial.pipex.com**

SGM Symposium Volumes

The contributions to the September 1999 symposium on *Transport of Molecules Across Microbial Membranes* are available as Volume 58 in the series. As usual, there is a 60% discount to members buying their personal copies. The prices are as follows:

- Members £26.00/$46.00
- Non-members £65.00/$115.00
- Student Member £16.00

The book can be ordered by post using the form in this issue of *Microbiology Today*. This form can also be used to order any past volumes in the series that are still in print.

Student Members wishing to purchase Symposium Volumes at the discount rate should write to the Grants Office at Marlborough House for a special order form.

CTI Centre for Biology

News of the Liverpool-based CTI Centre, which promotes the effective use of computers in biology teaching in tertiary education, has often appeared in this magazine. However, the days of the Centre are numbered. A recent review of the whole CTI system across the subject range has concluded that it should be re-structured. A new set of centres, the Learning and Teaching Support Network (LTSN), is to be established with a broader remit than the current focus on communication and information technology aspects of teaching. Each centre will also cover a broader range of disciplines than before. Bioscience will be expanded to include more applied areas such as forestry, agriculture and food science.

A bid for the LTSN Bioscience centre has been made by a consortium of the universities of Leeds, Liverpool and Aberdeen; the proposed lead site is Leeds under the directorship of Professor Ed Wood (Editor of *Biochemical Education*). Leeds would cover all the non-IT aspects of teaching while Liverpool would continue with its IT role. The subject areas would be divided between the three nodes. The first bid has been successful and a second phase bid has been submitted. If successful, the LTSN Bioscience will commence early in 2000.

Full details of the proposals are given in a report by Peter Miller, current director of CTI Biology, in the penultimate issue (Vol.10, No. 2) of the Centre's newsletter, *Life Sciences Educational Computing*.

Amongst the many other interesting articles in this publication is a review of an interactive practical on the web, *Introduction to Bioinformatics*, which may be particularly relevant to SGM members. The URL of the CTI Biology website is **www.liv.ac.uk/ctibiol.html**

SocietyNews

July Council Meeting

Search Committees for Council Officers

● Professor Dalton informed Council that progress was being made in the search for successors to Dr Goodwin as Scientific Meetings Officer and to Dr Roberts as Editor of *Microbiology Today*/ Publications Officer. Suggestions for his own successor as President would be considered by November Council.

Retiring members of Council

● Council expressed appreciation for the work done by the retiring elected members Professor Ron Hay, Dr David Hodgson and Professor Carlos Hormaeche. Professor Charles Penn was thanked for the excellent contribution he had made as an elected member for 3 years and then over a 5-year period as General Secretary.

Membership database

● The Executive Secretary reported that good progress had been made with the new membership database system, which would take over as the live operational system within a few weeks, after the final conversion of the data. He particularly wished to mention the part played by the Finance Manager, Richard Noble, in project management of this and the related new journal sales database, which was now operating successfully.

Budget for 2000

● The Treasurer's proposed budget for 2000 was approved, subject to ratification of membership subscription rates at the Society AGM in September.

Meetings questionnaire

● Council considered a preliminary analysis of responses. A full report of the findings is given in a separate article in this issue of *Microbiology Today* (see p. 179).

Publications

● Appreciation was expressed to the *Microbiology* editorial staff team for the work they had done in producing the special issue on streptomycetes, and to Dr Melanie Scourfield for the efforts she had made to ensure that the Symposium series volume on *Transport of Molecules Across Bacterial Membranes* would appear in time for the Leeds meeting. The Executive Secretary reported on progress with on-line publications of the Society's journals on HighWire, retendering the contract for journal printing in 2000 and recent developments in the E-biomed proposal from the US National Institutes of Health.

International affairs

● The International Secretary informed Council that a small number of applications for travel grants to attend the IUMS Congresses in Sydney was still being received, but that a considerable amount of the sum set aside was still unallocated. Council approved a request from the Congress organizers that funds be provided to support attendance at the Congresses by participants from developing countries.

● *Ron Fraser, Executive Secretary*

Group Committee Elections 1999

New Committee members, elected by postal ballot (Microbial Infection and Virus Groups) or elected unopposed (all other Groups) are as follows:

Cells & Cell Surfaces

C.D. O'Connor	University of Southampton
P. Rainey	University of Oxford

Clinical Virology

C. McCaughey	Royal Victoria Hospital, Belfast
P. White	PHLS, Norwich
J. Connell	Virus Reference Laboratory, Dublin
P. Molyneaux	Aberdeen Royal Infirmary

Education

A. Cann	University of Leicester
J. Verran	Manchester Metropolitan University
I. Davidson	Unipath Ltd, Bedford

Environmental Microbiology

D. Wynn-Williams	British Antarctic Survey, Cambridge
A. Ball	University of Essex

Fermentation & Bioprocessing

G. Hobbs	Liverpool John Moores University
N. Bainton	University of Surrey

Irish Branch

A. Bell	University of Dublin

Microbial Infection

M. Barer	University of Newcastle
P. Langford	Imperial College School of Medicine

Physiology, Biochemistry & Molecular Genetics

J. Gottschal	University of Groningen
N. Minton	CAMR, Porton Down
C. Rees	University of Nottingham

Systematics & Evolution

R. Goodacre	University of Wales Aberystwyth
I. Thompson	IVEM, Oxford
A. Ward	University of Newcastle

Virus

M. Harris	University of Leeds
I. Clarke	University of Southampton

SGM membership database

It has been brought to our attention that members have been receiving mailings which appear to originate from the unauthorized use of the SGM membership database. This database is not made available to any other organization or individual. However, SGM does carry out special mailings on microbiology-related products and services from carefully selected suppliers, to all members except those who have elected not to receive such separate mailings. If you have reason to believe that you receive mail which could only have originated from the unauthorized use of the SGM membership database, please forward as much information as possible, including the name and address of the organization sending out the mailing, to Janice Meekings at Marlborough House (j.meekings@socgenmicrobiol.org.uk).

New Members of Council 1999

Professor Alan Vivian (University of the West of England) commenced his 5-year term as General Secretary on 7 September 1999. A profile of Professor Vivian was published on p.128 of the August issue of *Microbiology Today*.

Following the recent ballot of Ordinary Members, the following have been elected to serve as Members of Council for a period of 4 years:

Professor Colin Howard (Royal Veterinary College, Camden, London), **Dr Dave Kelly** (University of Sheffield) and **Professor Ian Poxton** (University of Edinburgh).

Profiles of these new members will appear in the February 2000 issue of *Microbiology Today*.

News of Members

● **Dr Paul Bridge**, former principal scientist at CABI Bioscience, has been appointed Kew Professor of Mycology, a new post jointly funded by Birkbeck and the Royal Botanic Gardens, Kew.

● From 1 November 1999 **Dr Mark Pallen**, former Senior Lecturer in Medical Microbiology, St Bartholomew's and the Royal London School of Medicine and Dentistry, London, has been appointed Professor of Microbiology, Dept. of Microbiology & Immunobiology, The Queen's University of Belfast.

● The Society notes with regret the deaths of **Dr C.J. Bradish** (member since 1965), **Dr A.V. Garcia** (member since 1945) and of **Dr Roger Sherwood** (member since 1971).

Grants

Details of all Society grant schemes are available on the SGM website at **http://www.socgenmicrobiol.org.uk**

Most application forms can be downloaded. Any inquiries should be made to the Grants Office at SGM Headquarters, Marlborough House, Basingstoke Road, Spencers Wood, Reading RG7 1AE (Tel. +44 118 988 1821; Fax +44 118 988 5656; e-mail grants@socgenmicrobiol.org.uk).

President's Fund

The President's Fund provides small grants to younger members of the Society to assist towards travel worldwide to present their work at a scientific meeting, make a short research visit or attend an approved course. Applicants must be resident and registered for a PhD in a European Union country. Applications will also be considered from members in their first postdoctoral position, in cases where there is exceptional need. Grants from the Fund are awarded at the President's personal discretion.

The rules of the scheme are as follows.

- Applicants must be paid up members of the SGM for at least 3 calendar months before the date of their application for a grant.
- Applicants must be resident and registered for a PhD, or in a first postdoctoral position, in a country in the European Union.
- Limited support is available for the following:
  (a) Travelling to present a paper or a poster on a microbiological topic at a scientific meeting.
  (b) Making a short research visit.
  (c) Attending a short course (up to 2 weeks).
- Applicants must submit evidence of the oral or poster presentation at the meeting, or acceptance on the course or by the host institution, as appropriate with their completed application form.
- Applicants who are funded by a research council or other funding body that regularly supports conference attendance must submit evidence that they have applied for sponsorship from that body. Salaried applicants must submit evidence of their annual income (net, after tax).
- Grants are usually limited to £100 for attendance at meetings or institutions in the country of residence, £155 for travel to another European country and £220 for travel outside Europe (rates under review).
- Only one application may be made to the President's Fund during the term of a postgraduate studentship or first postdoctoral position.
- Retrospective applications will not be considered.
- TWO copies of the completed application form and all supplementary documentation must be submitted for consideration.

Postgraduate Conference Grants

Postgraduate Student Members of SGM currently resident and registered for a higher degree in the UK or another European Union country are eligible for a grant to cover the costs of accommodation and travel in attending ONE of the following Society meetings in 2000: **Surrey, January**; **Warwick, April**; **Exeter, September** or any other SGM Group or Branch meeting. Application forms giving full details of the scheme were sent to all Student Members in the EU with their subscription invoices. A copy can be downloaded from the SGM website.

Vacation Studentships 2000

The Society offers a limited number of awards to enable undergraduates to work on microbiological research projects during the summer vacation. The purpose of the awards is to provide undergraduates with experience of research and to encourage them to consider a career in scientific research. The studentships provide support at a rate of £135 per week for a period of up to 8 weeks. An additional sum of up to £400 for specific research costs may also be awarded. Applications on behalf of named students are now invited from SGM members in higher education institutions and research institutes. Details of the scheme are given below.

Rules

1. Applicants must be members of the Society working in a higher education institution or research institute in the UK or Republic of Ireland. Applications must be made on behalf of a named student. More than one application from a department/school will be considered, but in the case of several applications being submitted, departments/schools may be asked to rank the applicants.

2. Students must normally be in the penultimate year of their undergraduate course and registered at an institution in the UK or Republic of Ireland. Applications for students in their final year will not be considered. Medical students will be accepted at the end of their intercalated studies, but not during their elective period.

3. The research project must be on a microbiological subject. Studentships will not be awarded for projects that are part of degree work. A studentship may be held in a laboratory away from the normal place of study, but it must be located within the UK or Republic of Ireland.

4. Applications will be assessed by a Council Award Panel, based on the reports of two referees. The scheme is competitive and applications will be judged primarily on the scientific merits of the project and the suitability of the student. Once an award has been offered, it cannot be transferred to another student.

5. The awards will provide support for the student at a rate of £135 per week for a period of up to 8 weeks, and not usually less than 6 weeks. An additional sum of up to £400 for specified research costs may also be awarded. Grants are made to the institution to which the applicant belongs, not to the supervisor, on the understanding that it will administer the award.

6. It is a condition of the award that the student submits a brief report of the research at the completion of the studentship.

7. Applications must be made on the appropriate form, which is downloadable from the SGM website.

The closing date for applications is **25 February 2000**.

Seminar Speakers Fund 1999/2000

The purpose of this fund is to promote talks on microbiological topics in departmental seminar programmes. Applications are invited from higher education institutions where microbiology is taught for grants of up to £200 towards the travel, and if necessary accommodation, expenses of an invited speaker. Full rules of the scheme were published on p. 82 of the May issue of *Microbiology Today*. Applications will be dealt with on a first come, first served basis during the academic year, which is defined as running from September 1999 to June 2000. Written submissions should be sent to the Grants Office at SGM Headquarters.

IUMS/UNESCO/MIRCEN/SGM Fellowships

The fellowships provide an opportunity for young microbiologists from any developing country to participate in a research programme in a laboratory in a developed country. In 1998 SGM was pleased to offer sponsorship of US$4,000 for 2 years from its International Development Fund. Since the scheme began in 1997, 16 awards have been made to microbiologists from Mexico, Costa Rica, Cameroon, Cuba, Nigeria, Kenya, Senegal, Botswana, Romania, Iraq, Colombia, Belarus, India and China. See the SGM website for further details.

Good news for microbiology students

In the past Student Membership of the Society has been open to all full-time students (having no taxable income) who were resident and registered for a first or higher degree in a country of the European Union. Recognizing that UK undergraduate students have different requirements from postgraduates, Council decided to offer them a special category of membership. The residential requirements for postgraduate students were also reviewed and have been changed. These changes were ratified at the recent AGM of the Society.

Student Membership

● From now on Student Membership will be available to full-time postgraduate students anywhere in the world provided they have an interest in microbiology and are registered for a higher degree. They must also have no taxable income. The annual subscription is £20 or US$33. Student Members may purchase SGM publications at concessionary rates and pay no registration fees to attend Society meetings. Those resident in the European Union may also apply for Postgraduate Conference Grants and awards from the President's Fund.

Undergraduate Membership

● Undergraduate Membership is open to students resident and registered for a first degree, but only in the UK and Republic of Ireland. For the bargain subscription of only £10 Undergraduate Members will receive *Microbiology Today* and may attend Society meetings without payment of a registration fee. Careers events will also be held for them at different venues around the country. However, Undergraduate Members will not be eligible for travel or conference grants and will not be able to purchase Society publications at reduced rates. Information about this new category of membership is being circulated to all relevant UK university departments. An application form and full details are also available on the SGM website.

Undergraduate Microbiology Prizes

The new scheme to encourage excellence in the study of microbiology by undergraduate students has been very well received. Institutions offering an appropriate microbiology course were invited to nominate a student for an SGM prize, based on good performance in microbiology in the penultimate year of study for a BSc. The department was able to choose the type of assessed work for which the prize was awarded. Of the 70 departments circulated, 29 made nominations. Each prizewinner will receive a certificate, a cheque for £50 and free Undergraduate Membership of the Society for 1 year.

Undergraduate Microbiology Prizes will be awarded annually and the invitations for nominations in 2000 will be circulated next May.

SGM Membership Subscriptions 2000

The following rates were agreed at the AGM of the Society on 7 September 1999.

Ordinary Member	£	US$
■ Membership subscription (including *Microbiology Today*)	39.00	68.00
Additional concessionary subscriptions for publications:		
■ *Microbiology*	65.00	125.00
■ *Journal of General Virology*	65.00	125.00
■ *Int J Syst Evol Microbiol*	65.00	125.00

Student or Retired Member	£	US$
■ Membership subscription (including *Microbiology Today*)	20.00	33.00
Additional concessionary subscriptions for publications:		
■ *Microbiology*	32.00	60.00
■ *Journal of General Virology*	32.00	60.00
■ *Int J Syst Evol Microbiol*	65.00	125.00

Undergraduate Member	£	US$
■ Membership subscription (including *Microbiology Today*)	10.00	NA
No concessionary subscriptions to journals are available to Undergraduate Members		

Members are reminded that their 2000 subscriptions are due for payment by **1 December 1999**.

As in previous years, no journal or meetings information will be despatched to members who are in arrears, and there will be no guarantee of provision of back numbers of journals for members who pay their subscription late.

Payment by direct debit or continuous credit card

Subscription notices were despatched recently to all members paying by direct debit or by continuous credit card arrangement. To continue your present status and journal requirements, no further action is necessary. However, if you pay by continuous credit card, you should check that the card number and expiry date on the subscription notice are correct. To change your membership status or journal requirements for 2000, or your credit card details, you should have amended your subscription notice and returned it to the membership office by **14 November 1999**. However, if you have missed this deadline, your amended notice will be accepted if it is submitted immediately.

Payment against invoice

Invoices were despatched recently to all members who pay by this method. If you did not receive one, please inform the Membership Office.

Subscriptions waived for unemployed members

As in previous years, subscriptions may be waived at the discretion of the Society for unemployed members under the age of 35 who are resident in the UK. If you are eligible and wish to benefit in this way in 2000, you should send a signed statement that you are currently unemployed to the Membership Office before **30 November 1999**. (Please note that no increase in journal requirements will be permitted.)

Income tax relief on membership subscriptions

Members who are liable for UK income tax are reminded that their annual subscriptions to the Society have been approved by the Inland Revenue as qualifying for income tax relief. Any member who would like further information or has difficulty in obtaining this relief should contact the Executive Secretary.

SGM meetings and activities survey results

Pat Goodwin & Ron Fraser

In May this year, a questionnaire about the Society's meetings and other activities was sent to all members; responses were received from 30% of those in the UK and 18% of those living abroad. This represents a very satisfactory response rate for a survey of this type and we are grateful to everyone who took part.

Groups

Members were asked to indicate which of the Society's Groups matched their scientific interests. The results are shown in Fig. 1 and give an indication of the size of the 'supporters' club' for each Group. Only about 10% of respondents commented on possible new Groups or changes in Group structure. The commonest suggestions for new Groups were in the areas of clinical bacteriology, food and industrial aspects.

Other societies

Sixty-eight percent of respondents were members of at least one other society, the commonest being the American Society for Microbiology, Society for Applied Microbiology, Biochemical Society, British Society for Immunology, Genetical Society and Pathological Society. In all, over 100 other societies were mentioned.

Meetings

The series of questions about meetings produced a wealth of information. Fig. 2 shows the numbers of meetings attended by members over the last 5 years and, not surprisingly, indicates a spectrum from the minority who had not attended any, to those who had attended several. Attendance was higher for UK members than for those from overseas. At first sight, these meeting attendance figures may seem low, but when grossed up to the scale of the full membership, they indicate an average of 2,000 meeting attendances per year, which is very close to what we observe in real life.

It was very gratifying that 95% of respondents were either satisfied or very satisfied with the scientific content and quality of the meetings, and with facilities and value for money. But we will continue to aim for 100% satisfaction and are constantly seeking ways to improve.

The cost of accommodation was considered to be more important than the cost of food, and the maximum amount that people were prepared to pay for 24 hours food and accommodation varied widely, presumably in reflection of differences in the extent to which people receive financial support for attendance. The majority of respondents (73%) were willing to travel any distance to a destination in the UK to attend meetings. However, a number of written comments emphasized the importance of good facilities and accommodation, and locations where there were other things to do as well as the meeting itself. Some of the universities which have provided less than wonderful accommodation, food and other facilities in the past were duly recognized, and no, we will not be going back to them. We increasingly look to use universities which approach conference business in a properly professional manner. Respondents were split 3:1 in favour of continuing to use university venues, as opposed to conference centres such as Brighton or Harrogate.

The big question was about how the Society should set out its annual pattern of meetings. There was a 3:1 split in favour of continuing with the present pattern of three main meetings in April, September and January. However, there was also strong support (2.3:1) for two

Fig. 1. Numbers of supporters of the Society's special interest Groups (from a poll sample of 1184 members)

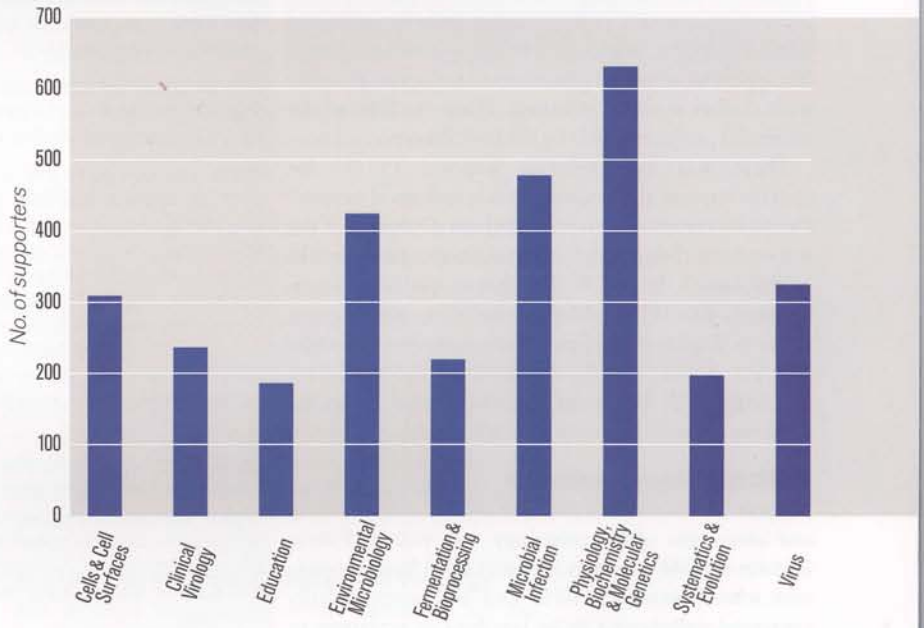
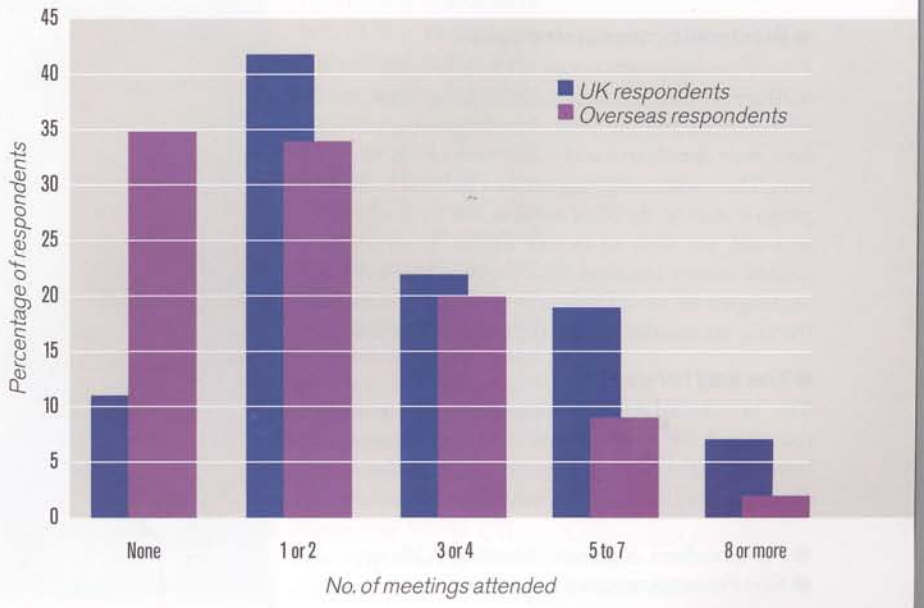


Fig. 2. Frequency of attendance of members at Society meetings over the last 5 years



meetings, in April and September. As the Group committees have already largely voted with their feet by deciding not to arrange symposia at January meetings after Guildford in 2000, it is likely that the two-main-meeting pattern will prevail, although Groups could continue to arrange stand-alone or joint meetings with other societies at other times. There was little support for a two-meeting model at other times of year.

The main alternative suggestion, that the Society should hold a single large meeting in spring, received a 2:1 vote against. Written comments suggested a degree of polarization, with respondents either strongly in favour or strongly against. There was very little support for a single meeting at another time of year. There did appear to be support for amplifying the main meetings programme with shorter regional meetings, along the lines of the successful programme run by the Irish Branch.

There was overwhelming support (97%) for continuation of the main symposia and good support (76%) for continuing to publish them. Only half of the respondents thought that more main symposia should be published, but 81% felt that specialized Group symposia should be published, if dealing with topical subjects. Eighty-eight percent of respondents thought that the Society should be involved in more joint meetings with European microbiological societies; numerous possible partners were mentioned.

● Microbiology promotion

Support for activities to promote public understanding and awareness of microbiology was varied. Public lectures at SGM meetings appealed to 73% of respondents, schools lectures to 64%. One-half of respondents expressed willingness to be involved in activities to promote public understanding and 38% would be willing to handle enquiries from the media.

● Electronic communications

Finally, on communications, 82% of respondents were willing to enter their contact details in a voluntary on-line address book and the same percentage were willing to have their details in a wider directory of UK life scientists. There was strong support for a bulletin board/news group feature on the SGM website, but 33% of respondents did not wish to receive e-mail messages about general Society business. This suggests that any e-mail alerting service would have to be on a sign-up basis rather than run automatically from the membership database.

● The way forward

The broad findings of the survey have now been considered by Council and the Group conveners' committee. The clear opinions expressed by members are already playing their part in shaping future developments.

● Pat Goodwin, Scientific Meetings Officer
● Ron Fraser, Executive Secretary

MISAC Competition 1999

■ Make a meal with microbes

For many years the Microbiology in Schools Advisory Committee, whose secretariat is based at Marlborough House, has run successful competitions for school pupils in the 11–16 age range. Various aspects of microbiology have been covered and pupils are asked to produce either posters or leaflets, depending on the topic.

This year the pupils were asked to create a menu for a nutritionally balanced meal (up to four courses) to include a wide variety of ingredients produced with the help of microbes. This had to be in the form of a wall chart to inform catering staff in canteens and restaurants about the beneficial uses of microbes in food and drink. Each item in the menu had to be annotated to explain the role of microbes in its production.

The competition was sponsored by Yakult who sent two of their nutritionists to participate in the judging process with MISAC members at Marlborough House.

There was once again a large number of entries, over 200 from 35 schools. The quality was very high with some extremely diverse and well balanced menus that highlighted the varied role that microbes play in the production of our food. Both traditional and new technologies were mentioned. Foodstuffs ranged from edible fungi through to legumes, dairy products and bread, whilst wine or beer, of course, complimented by coffee, were on many bills of fare. Many were delightfully illustrated and the judges had the usual difficult task of picking out the best.

The entries were judged in two age groups: 11–14 and GCSE/Standard Grade. The winners displayed accurate knowledge, well annotated diagrams and imaginative menus that would have been a pleasure to eat. Both hand drawn and word-processed wall charts featured amongst the winning entries. First prize was £100 for the school and £30 for the pupil. Second and third prizes were also awarded.

The winner of the 11–14 class was Zara Edwards from Shrewsbury High School and the joint winners of the GCSE age range were Felicity Miller, Claire Ingram and Stephanie Carter from Northampton School. MISAC member Margaret Whalley travelled to Shrewsbury to present the prize to Zara at a school assembly. This event was reported in the local press. The school has already spent a portion of its prize money on equipment to carry out antibiotic testing and they hope to purchase a bubble logger with the remainder. Unfortunately, it did not prove possible to make a presentation at Northampton School.

Every pupil entering the competition was sent a certificate and the schools received a pack of relevant microbiology teaching materials.

Next year's competition for the millennium will feature vaccination. Sponsored by the British Society for Immunology, Don Whitley Scientific and FEMS, this promises to attract a bumper crop of entries as it is an important topic in the UK National Curriculum at Key Stage 3. Students are being asked to create a public information leaflet for parents explaining how immunization provides their children with protection against disease. The closing date is **31 March 2000**. Full details are available on the SGM website.

What is MISAC?

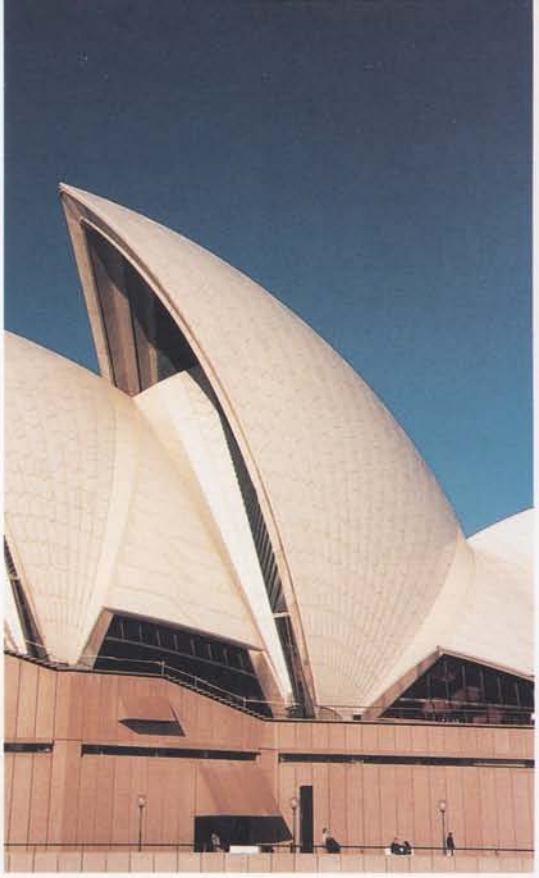
The Microbiology in Schools Advisory Committee is made up of representatives from a wide range of educational institutions and scientific organizations. Currently it is sponsored by the SGM, SfAM, CLEAPSS, BMS, Institute of Biology, The Wellcome Trust, SAPS and the NCBE. The IoB kindly provides MISAC with a meeting room. MISAC is committed to promoting the teaching of microbiology in schools. As well as running the annual competition it provides advice on the safe use of micro-organisms, makes representations to national science education bodies, maintains contact with examination boards and produces teaching resources and factsheets. Details of MISAC activities may be found on the SGM website. The secretariat of MISAC is based in the External Relations Office at Marlborough House. Please contact **Janet Hurst** or **Dariel Burdass** for further information.

Going Public packs

If you are organizing an event during SETweek to promote the public understanding of microbiology, or are going out to give a microbiology lecture to schools or running any similar activity, don't forget that factsheets are now available from the SGM to help you to communicate your science to the public safely. Compiled by Education Officer Liz Sockett, there are three sheets in the *Going Public Pack*: Going Public with adult groups, Going Public with teenagers and Going Public with 5–12-year-olds. e-mail **d.burdass@socgenmicrobiol.org.uk** if you would like a set.

IUMS Congresses

Janet Hurst



The 1999 Congresses of the International Union of Microbiological Societies (IUMS) were held in Australia in August. The Sydney Convention and Exhibition Centre, located in the stunning setting of Darling Harbour, proved to be an excellent venue. The area has been extensively renovated in the past 10 years and the waterfront, with its cafés, shops, museums and ferries, not to mention the Casino and nearby Chinatown, offered tempting diversions from the conference programme, especially as the sun shone so brightly in what the Australians term 'winter'. Straying delegates were easily recognized by their bright yellow and blue conference rucksacks amongst the throngs of people of all ages and nationalities!

The XIth International Congress of Virology was on first, from 9–13 August; the IXth International Congress of Bacteriology and Applied Microbiology and IXth International Congress of Mycology ran during the second week (16–20 August), but many committee meetings and special workshops, including a timely one on 'Bioterrorism', were held in the interval between the congresses. For those requiring a break from the scientific activities, a range of tours and social events was available. A social programme had also been arranged for every weekday evening.

The Australian Society for Microbiology, who hosted the meetings and made ICBAM their own annual conference, were delightfully friendly and hospitable. No-one will forget the 'Australiana Nights' with their seemingly inexhaustible supplies of wine and Oz food specialities, and entertainment which included sing-songs (*Waltzing Matilda*, of course), whip-cracking demonstrations, sheep shearing and the unmissable opportunity of stroking a wombat. Hopefully none of the delegates fell into the fountains of Darling Harbour staggering back to their hotels.

Every effort was made by the organizers to provide a memorable time for the delegates, both scientifically and socially. The congresses were run very efficiently and thanks are due to all concerned. Particular credit is due to John Mackenzie, who as overall chair for the scientific organizing committees, worked untiringly for many years to make the congresses a success.

SGM input

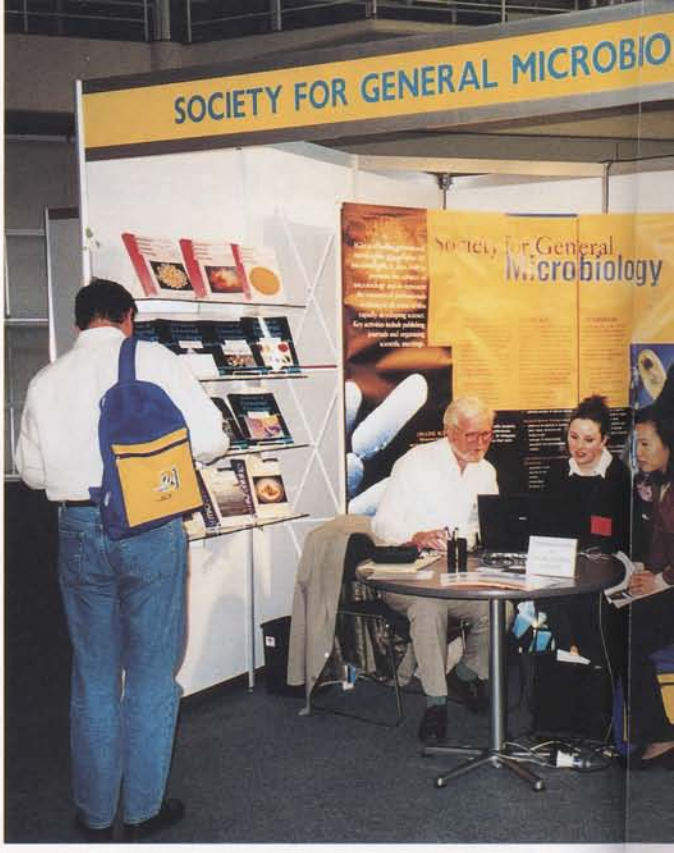
The Society has been closely involved with these congresses from the very start 7 years ago. Successive SGM International Secretaries Tim Gray and Jeff Almond played pivotal roles in organizing the scientific programmes for ICBAM and ICV, respectively, and the events have been widely promoted through Society meetings and publications. The Society also provided significant sponsorship, both directly and by offering travel grants to delegates from the UK. SGM sponsored the closing plenary session of ICV and the opening plenary session of ICBAM.

XIth International Congress of Virology

ICV opened with a spectacular ceremony on the Sunday evening. After national songs from the Australian Youth Choir, Jeff Almond, chairman of the ICV Programme Committee as well as SGM International Secretary, welcomed delegates on behalf of the Virology Division of IUMS. He described the highlights of the first 100 years of the discipline and the important role it plays in the development of all biosciences. Many more speeches followed from virologists of international renown, culminating in an address by D.A. Henderson of CDC, on the theme 'An impending World Cup – man vs virus'. D.A.'s achievement in eradicating

ABOVE:
Sydney Opera House.
PHOTO AIDAN PARTE

LEFT:
The Sydney Conference and Exhibition Centre and Sydney Harbour.
PHOTO RON FRASER



Congress facts

		ICV	ICBAM/ICM
Participants			
	Total	2429	1378
	Delegates	1407	781
	Students	334	233
	Speakers	379	140
	Accompanying persons	202	79
	Exhibitors	90	126
	Top four delegations	USA 380, Japan 181, UK 170, Germany 105	Information not supplied
Papers			
	Invited	51	Information not supplied
	Offered oral	611	Information not supplied
	Posters	1100	ICBAM 395, ICM 217

SGM awards and fellowships

110 SGM International Congress Travel Grants were awarded to enable UK scientists (including postgraduate students) to go to Sydney. Council was also pleased to accede to a request from the Congress organizers for further sponsorship to permit the attendance of microbiologists from developing countries. A contribution of £23,500 was made which provided fellowships to the following people.

- Professor Ahmed Yousief Gibriel, Cairo, Egypt
- Professor Krassimir Metodiev, Varna, Bulgaria
- Ms Olga Miatleva, Moscow, Russia
- Professor N. Parasakthi, Kuala Lumpur, Malaysia
- Dr N.P. Sunil-Chandra, Ragama, Sri Lanka
- Dr C. Chanyasanha, Bangkok, Thailand
- Dr Oleg Zhirnov, Moscow, Russia
- Dr Irina Zubkova, Odessa, Ukraine
- Dr Irina Kolssova, Odessa, Ukraine
- Dr Gerardo Guillen, Havana, Cuba
- Mr Arnab Basu, Calcutta, India
- Dr Swarabjit Singh, c/o Pennsylvania, USA
- Dr June Busingye, Kampala, Uganda
- Dr J. Shanmugam, Trivandrum, India
- Dr Shailesh Dewasthaly, Pune, India
- Professor M.J. Cardosa, Sarawak, Malaysia
- Dr T. Konakova, Moscow, Russia

A condition of their award was the fellows joined the Society; but as a gesture of goodwill to mark the start of the new millennium, the subscription for 2000 will be complimentary.

smallpox as Programme Director for the WHO, assisted by the venerable Australian virologist Frank Fenner, was then marked by the presentation of a citation to these two distinguished scientists. At the end of the ceremony the delegates all streamed to the exhibition hall where wine and cheese awaited them.

The sessions that followed over the next 5 days covered a wide range of current topics in virology. There were plenaries each morning and parallel workshops in the afternoons. Most of the great names in virology were present, including four Nobel laureates. The prestigious Stuart Mudd Lecture was delivered by Hilary Koprowski.

IXth International Congress of Bacteriology and Applied Microbiology & IXth International Congress of Mycology

Once more the delegates were treated to an opening ceremony with entertainment from young Australians before the speeches. Dick Groot Obbink gave the welcome address followed by a number of presentations to distinguished microbiologists, including the Van Neil and Arima awards and annual awards of The Australian Society for Microbiology to its own members. Rita Colwell's keynote lecture 'Marine microbiology – the ocean frontier' held the audience spellbound, blending modern molecular science with the diversity of microbial life, particularly that found in deep-sea vents. Delegates then made their way to the exhibition hall for the welcome reception.

ICBAM and ICM followed a different pattern from ICV, with ICBAM plenaries each morning, symposia/workshops in the afternoon and ICM plenaries after lunch with their offered paper sessions in the morning. There was the same wide range of topics, including a symposium on *Helicobacter*, an organism which was first cultured in Australia. Sadly the congresses did not attract as many delegates as ICV, although there was a much larger trade show, and consequently there was not the same 'buzz'.

View from Stand 181

In recognition of SGM's role as a significant sponsor, we were invited to take a stand in the trade exhibition for the whole duration of the congresses.

Thus it was that Ron Fraser and Janet Hurst from Marlborough House found themselves in Sydney for 2 weeks in August, setting up and manning the SGM stand. In the second week they were ably assisted by Aidan Parte, Managing Editor of the *International Journal for Systematic Bacteriology*, who was there both to promote the journal and to attend an editorial board meeting. IJSB is a dynamic publication which is to be issued bi-monthly in 2000 under the new name *International Journal of Systematic and Evolutionary Microbiology* (IJSEM).

On the stand we had a display of copies of recent SGM journals and symposium volumes and gave away back issues of *Microbiology Today*, membership literature, meetings information and a selection of educational resources. On-line demonstrations of the electronic versions of the journals and the Society website were available on a notebook computer. This also enabled us to keep in touch with SGM headquarters by e-mail.

The exhibition hall also housed the posters and was where the delegates took their tea and coffee. This ensured that there was a constant stream of people passing through the trade show. Our stand was well placed for obtaining refreshments at all times! The welcome receptions also took place in the hall.

The other exhibitors were a mixture of microbiological organizations (ASM, SfAM, the Australian Society, FEMS, etc.), laboratory suppliers, publishers and local companies promoting the tourist trade or products like opals. Some attracted attention by providing food – the hamburgers being barbecued by a certain well known pharmaceutical company will not be appearing at SGM meetings! However, the fruit juice on tap on another stand was more than welcome.

The main impressions were of great friendliness and goodwill. The delegates were a cosmopolitan crowd and it was interesting for us to meet people from so many other countries, especially from the Pacific Rim whom we do not usually encounter. A few very familiar faces from home included our President Howard Dalton, ex-Treasurer Allan Hamilton and quite big contingents from CAMR and UKNCC.

There was much interest in the SGM and its publications. Several delegates joined on the spot, others took away promotional literature. Our educational posters were very popular and should be decorating walls in laboratories and classrooms throughout the world as a result. We were pleased to chat to existing members, especially those from Australia, who do not normally attend our meetings. There were quite a lot of Australian undergraduate students present, with the usual problems of finding jobs and studentships. Advice was keenly sought on employment possibilities in London.

Overall it was excellent exposure for the SGM and our attendance was well worthwhile. The staff made some useful contacts. We look forward to the next IUMS Congresses in the Palais des Congres, Paris, 27 July–1 August 2002.

● *Janet Hurst, SGM Deputy Executive Secretary*

ABOVE:
Sydney Harbour Bridge at sunset (top) and the Sydney Conference and Exhibition Centre (bottom).
PHOTOS AIDAN PARTE

ABOVE (CENTRE PAGE):
The SGM stand at the 1999 IUMS Congresses in Sydney.
PHOTO JANET HURST

LOWER LEFT:
A view of Sydney and Circular Quay from the harbour.
PHOTO AIDAN PARTE

Meetings

Meetings on the web

Up-to-date information on future Society meetings is available on the website http://www.socgenmicrobiol.org.uk

Meetings organization

The programmes of the Society's meetings are organized by the committees of the special interest groups, co-ordinated by the Scientific Meetings Officer, Dr Pat Goodwin. Suggestions for topics for future symposia are always welcome. See p. 204 for contact details of Group Conveners. Administration of meetings is carried out by Mrs Josiane Dunn of the Meetings Office at SGM Headquarters, Marlborough House, Basingstoke Road, Spencers Wood, Reading RG7 1AE
Tel. 0118 988 1805
Fax 0118 988 5656
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Abstracts book

Leeds Meeting September 1999

The full text of the abstracts book is now available as a PDF file on the SGM website.

Winter 2000

● Virus Infection – Life or Death for a Cell

University of Surrey, Guildford
5–7 January 2000

145th Ordinary Meeting

Virus and Clinical Virology Groups

The meeting will contain 14 plenary talks (40 minutes plus 5 for questions), open paper sessions and evening workshops. The invited speakers will review the process of programmed cell death (apoptosis) and the mechanisms by which a variety of viruses subvert this normal cellular pathway. The mechanisms by which viruses transform cells and induce cancer, and establish latent or persistent infections will also be addressed. This programme should appeal to all virologists with clinical or basic research interests, as well as cell biologists with interests in apoptosis, cell transformation and cancer.

● PROGRAMME BOOKLET
A booklet giving full details of the programme and a booking form is enclosed with this issue of *Microbiology Today*. Any changes will be posted on the SGM website.

● OFFERED POSTER PRESENTATIONS
Will delegates whose offered posters have been accepted please note that an area of **1m x 1m only** is available on the poster boards for their display.

● MICROSCENE NOTICEBOARD
At the meeting, a board will be set up with notices of jobs, postdoctoral positions, studentships, courses, conferences etc. Contributions are welcome and may either be brought to the meeting or sent beforehand to Janet Hurst at Marlborough House.

Offered Papers

Offered posters are welcome but each one should be associated with a Group. General Offered Posters will no longer be accepted. Titles and abstracts should be sent to the appropriate Convener, preferably by e-mail. The subject content should be relevant to the remit of the Group (see website for details); it does not have to relate to the topic of the Group Symposium taking place at the particular meeting. Abstracts are required in a standard format – see website for details or contact the Events Administrator.

Promega Prize

- Are you a member of the SGM?
- under 28 years of age?
- a postgraduate or first postdoc?
- thinking of presenting an offered paper or poster at an SGM meeting?

Why not enter for the Promega Prize Competition? You could win £200 in the SGM section of the competition and go on to compete for a further £2000 in the *Young Life Scientist of the Year* event. Contact the Meetings Office or see website for details.

Future Meetings

SPRING 2000 – Millennium Meeting
University of Warwick, 10–14 April 2000
(jointly with Society for Applied Microbiology)

● Main Symposium (10–11 April)
Fighting Infection in the 21st Century

Organizers: P. Goodwin, P. Andrew, G. Smith, D. Stewart-Tull, M. Easter and P. Oyston
A leaflet about the meeting is enclosed with this issue of *Microbiology Today*.

● Other Symposia

● 11–12 April – Potable water treatment
Fermentation & Bioprocessing Group and SfAM
Contact: Reg England (r.england@uclan.ac.uk)

● 12 April – Microbial ecology of food-poisoning micro-organisms
Environmental Microbiology Group and SfAM
Organizers: Linda Lawton (l.lawton@rgu.ac.uk) for SGM and Andy Davies (SfAM Food Group).

● 12 April – Transcriptional control circuits in fungi
Physiology, Biochemistry & Molecular Genetics Group
Organizer: A. Brown (al.brown@abdn.ac.uk)

● 12 April – Vaccine delivery
Microbial Infection Group
Organizer: P. Oyston (poyston@hotmail.com)

● 12 April – Public education in safe water and food
Education Group and SfAM
Organizer: R. Bishop (rh.bishop@ulst.ac.uk) for SfAM

● 12–14 April – Virus entry and exit
Virus Group
Workshop submissions to the appropriate organizer (see website) by **28 February 2000**.
Titles/abstracts to the organizer Geoff Smith (glsmith@molbiol.ox.ac.uk) by **3 December 1999**.

● 13–14 April – Molecular epidemiology: infrasub-specific classification and identification
Systematics & Evolution and Clinical Virology Groups
Organizers: Gerry Saddler (g.saddler@cabi.org) and Tim Wreghitt (tim.wreghitt@msexc.addenbrookes.anglox.nhs.uk)
16 invited speakers working on a range of clinically significant organisms will discuss the topic using examples taken from bacterial, fungal, protozoal and viral infection. Poster titles with a 200 word abstract must be submitted to one of the organizers by **3 December 1999**.

● 13–14 April – Proteases, proteolysis and control
Physiology, Biochemistry & Molecular Genetics and Cells & Cell Surfaces Groups
Organizers: C. Stirling (colin.stirling@man.ac.uk) and D. Hodgson (dm@dna.bio.warwick. ac.uk)

● OTHER EVENTS: evening workshops, social events, trade exhibition.

● Up-to-date details of all sessions are available on the SGM website. A booking form is on p. 205 or may be downloaded from the web.

● OFFERED POSTERS: the deadline for receipt of titles/abstracts is **3 December 1999**.

Biotechnology in Europe: ECB9

John Grainger & John Bonham-Carter

The 9th European Congress on Biotechnology was held in July at the Heysel Congress and Exhibition Centre, Brussels. It consisted of science and technology sessions, poster displays, a trade exhibition with about 50 exhibitors (BIOtop99) and, being the 95th European Federation of Biotechnology (EFB) event, the meetings of the various EFB groups. Support came also from the Commission of the European Communities, the Directorate General for Technologies, Research and Energy for the Walloon Region and the Ministry of Economic Affairs for the Brussels Region.

The formalities of the opening day included a customarily weighty salvo from Arnold Demain (MIT, USA) on the power and potential of the microbe in the biotechnology business and an evening of libation from a fair range of Belgian beers, courtesy of Interbrew.

The main academic business of the congress consisted of 4 days devoted to nine simultaneous, widely ranging symposia and an additional session each evening. Three symposia: Agriculture and food; Environment; and Animal and human health each consisted of two parallel sessions. The other six were: Chemicals manufacturing; Engineering and manufacturing; Information modelling and control; Life sciences; Physics and chemistry; and Social and economic dimensions. At first glance, each symposium appeared to have a full programme which presented the usual task of having to make hard choices about what to attend. However, the problem eased considerably when more careful examination revealed that the programmes of the six symposia were very substantially bolstered by double entries. It was particularly noticeable that the 'buzz' usually to be expected of an event attended by some 1,500 delegates was lacking, perhaps because of the diluting effect of the sessions and exhibition taking place in three adjacent buildings.

From the UK, both Birmingham University and UCL were well represented, with Dr Titchener-Hooker outlining the advances being made at UCL with ultra-scale-down operations and disposable plastic technology. An interesting lecture was given by Thomas Bachiner of Stockholm University working in conjunction with Pharmacia and Upjohn. Using an electronic nose as an on-line fermentation monitor for the production process, their team predicted a contamination at least a day before standard sensors could detect the problem. Despite well-known problems with sensor array technology, it looks likely that this area will receive an increasing amount of attention. Unfortunately, due to overlap with a conference in China, some control experts were not present, but it was pleasing to see that Dr Sydall (Birmingham) and Dr Glassey (Newcastle) were both cited for recent work on control.

On the final evening of the conference an impromptu 'Happy Hour' was held, but when it was realized that the orders for delivery of beer and soft drinks must have been muddled, rumours soon spread through the crowd that this was perhaps an 'Unhappy Hour'. Delegates headed rapidly for the delights of the restaurants and bars in beautiful Grande Place and its alleys to sample the range of delicious Belgian food on offer.

Reflecting on the week, the presence of few recognized names and faces from Microbiology UK reinforced the impression gained before the event that advance publicity had not penetrated very deeply over here. There were some good sessions but, not unexpectedly, the attraction and value of the congress suffered from its breadth and registration fee, a far cry from the only time that it took place in the UK – ECB2 in Eastbourne in 1981. Despite this, European networking opportunities were excellent and we at Adaptive Biosystems at least left invigorated.

● *Dr John Grainger, Reading University*
● *Dr John Bonham-Carter, Adaptive Biosystems Ltd*

International Development Fund report

Culture Collections in Cuba

■ Gladys Pérez de la Fuente

Micro-organisms are essential for the maintenance and functioning of global ecosystems and are a vast resource that can be exploited by man. The conservation of these organisms is a scientific necessity as a source of invaluable reference material for future generations. Unfortunately, *in situ* conservation of microbial cultures is uncertain, so culture collections (*ex situ* conservation) play a vital role in maintaining microbial diversity. In addition, they can supply cultures that are needed by educational, scientific and industrial communities.

In Cuba, the first collections were established in 1964 and have continued to increase. In May 1995, the first workshop, 'Organisations and preservation of a bank of industrial strains', was held in our country. The participants agreed to work on the establishment of the Cuban Federation of Culture Collections. As an interim measure, it was agreed to form an ad hoc National Group of Microbial Culture Collections to exchange information and develop a Cuban network. This group has no official power over its members, but it is the result of the voluntary union of all these collections based on their common interests.

The National Group comprises a Steering Committee and representatives of more than 37 Cuban institutions. The members are scientists working directly with, or who are interested in collections of micro-organisms, cell lines and other biological materials (plasmids, hybridomas, etc.). It meets quarterly and has devised an action plan. As a result different activities have developed, among which the first workshop and first course on 'Microbial

LEFT:
The 'National Hotel' in Havana, Cuba – '*the*' place to stay.
PHOTO P.N. GREEN

culture collections' (in 1996 and 1997, respectively) stand out. At the end of 1997 the National Group of Cuban Culture Collections was affiliated to the National Commission of the Genetic Resources for Agriculture and Food and together they have initiated a forum to discuss micro-organisms and their management in Cuba.

In 1998 the 'Information Centre for Cuban Culture Collections' was initiated, proposed by the National Group. It has several objectives: to centralize information from Cuban collections and create a corresponding database, and establish a bank of specialized documents regarding collection work donated by organizations, collections and individual specialists around the world. In future we intend to develop directories and listings of national strains, as well as publishing related articles.

In 1999, thanks to Dr Peter N. Green, curator of the National Collection of Industrial Food and Marine Bacteria, Aberdeen, UK, SGM International Development Fund support was obtained to help Cuban Culture Collections begin to achieve some of these objectives. As a result of this generous award, a computer and reference books are now available for Cuban Culture Collection work. Also, in April of this year as part of the grant programme, I was able to visit several relevant members of the UK Culture Collections network (including the National Collection of Industrial Food and Marine Bacteria, Culture Collection of Algae and Protozoa, CABI Bioscience UK Centre, Microbial Strain Data Network and National Collection of Type Cultures). Visiting these collections afforded me an invaluable opportunity to study at first-hand a range of collection management skills, including preservation, identification, databases, packaging and postal regulations and quality assurance.

In addition, thanks to Dr David Smith, UKFCC President, and financial support from MSDN, I was able to participate in a UKFCC training course on the 'Preservation and maintenance of micro-organisms and cell cultures' that took place on 26–28 April 1999 at the CABI Bioscience Centre. This examined preservation methods used on a wide range of micro-organisms.

In summary, the visit was very useful in that I was able to obtain a background of information on the work of culture collections and it was also enjoyable from a personal point of view. I now have the moral and scientific responsibility to do my best to convey to the members of the National Group of Cuban Culture Collections all that I was able to learn on my visit to the UK. One of the next steps will be to try to organize an expert group to expand upon the practices learnt. I will also begin to co-ordinate a national database.

Finally, I would like to recognize and thank the SGM, the UK Culture Collections curators and staff, and particularly Dr Peter Green for giving me this great opportunity and for helping Cuban Culture Collections.

● *Gladys Pérez de la Fuente MSc works at the Instituto de Oceanologia, Havana, Cuba*

ABOVE:
The author on a roof overlooking Havana.

OPPOSITE PAGE:
The author (left) with two of her colleagues outside the Instituto de Oceanologia in Havana.

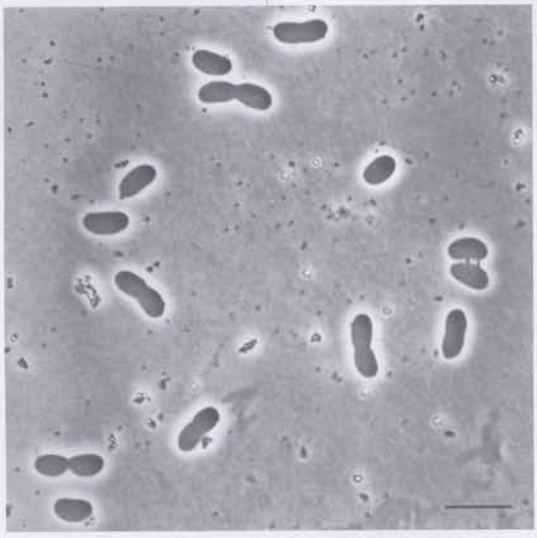
PHOTOS P.N. GREEN

Hot off the Press

Science journalist Meriel Jones takes a look at some papers in current issues of the Society's journals which highlight new and exciting developments in microbiological research.

ABOVE RIGHT:
A collaborative Japanese/Chilean survey of HTLV-I in Chile included an excursion to Easter Island, the Polynesian island closest to the South American mainland.
COURTESY ERIC MEOLA/THE IMAGE BANK

BELOW:
Phase contrast photomicrograph of *Desulfofaba gelida* strain PSv29^T. Bar, 10 µm.
COURTESY C. KNOBLAUCH, MAX-PLANCK-INSTITUTE FOR MARINE MICROBIOLOGY, BREMEN, GERMANY



Arctic sulfate-reducers

The inorganic chemistry of sulfur supplies energy to some bacteria. They reduce sulfate to hydrogen sulfide as they respire, in a manner similar to our conversion of oxygen to water as we breathe. Sulfate-reducing bacteria (SRBs) thrive in ecological niches not available to oxygen-requiring organisms. One habitat is the mud on the sea floor covering over two-thirds of the planet. These cold sediments lack oxygen, but are rich in minerals and organic materials that drift down through the water. Indeed, current estimates suggest that SRBs recycle half the organic carbon in marine sediments.

Almost all the known SRBs grow in warmth, but not at 4 °C or below, which is a typical temperature of the ocean's depths. The SRBs in these deep ecosystems must be able to grow at low temperatures. The question of how similar the cold-loving, marine SRBs are to their warmth-demanding relations has now been partly answered by researchers at the Max-Planck-Institute for Marine Microbiology in Bremen, Germany. They have isolated SRBs from Arctic mud scooped up off the coast of Svalbard in northern Norway, in water temperatures down to −1.7 °C. They took the precaution of keeping the sediments cold and oxygen-free as they rapidly put samples into laboratory growth media on the deck of the ship.

Back in the lab, and after several months work, they ended up with 30 different pure cultures of SRBs that had never experienced a temperature above 10 °C. They then put five cultures through a battery of metabolic tests. Since previously known SRBs grow very slowly, the researchers waited up to a year to be sure of some test results. However, their patience was rewarded by discovering that the strains had a whole series of differences, from both other bacteria and each other.

The new strains were united by an ability to grow well below 0 °C. However, other key characteristics of SRBs split them into three groups with features such as a cellular fat composition which had never been seen before. After putting all the data together, the researchers were confident that they had obtained the first members of three new genera of bacteria that might dominate the ecology of cold sea sediments.

C. Knoblauch *et al.* Psychrophilic sulfate-reducing bacteria isolated from permanently cold Arctic marine sediments: description of *Desulfofrigus oceanense* gen. nov., sp. nov., *Desulfofrigus fragile* sp.nov., *Desulfofaba gelida* gen. nov., sp.nov., *Desulfotalea psychrophila* gen. nov., sp.nov. and *Desulfotalea arctica* sp. nov. *Int J Syst Bacteriol* 49, 1631–1643.

Whipple's disease – linking symptoms with strains

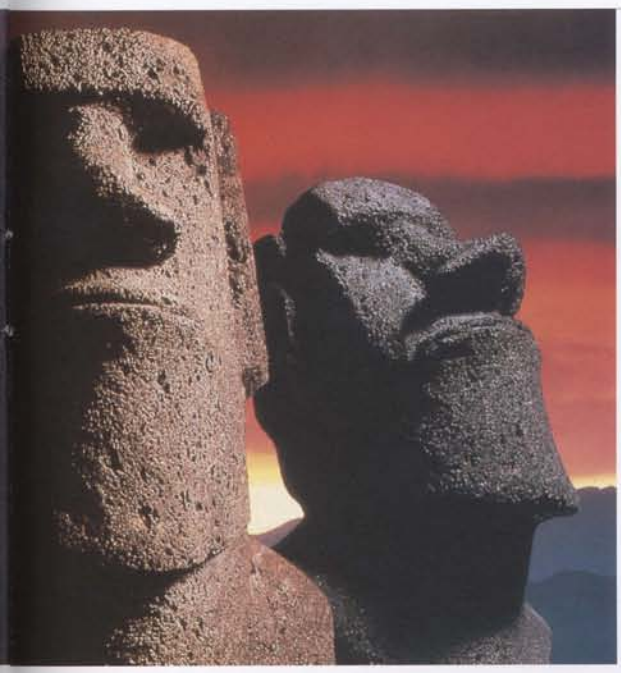
The classic way to prove that a particular micro-organism causes a disease involves isolating a pure culture of the suspect microbe and then inoculating it back into a susceptible host. The case against the microbe is usually considered proved if typical disease symptoms develop. This procedure was developed by Robert Koch in the late nineteenth century. A key feature in proving Koch's postulates, as they are now called, is the need to grow the microbe in a pure culture. It has been very difficult to grow the causal agents of some diseases in the laboratory, but molecular biological techniques can now provide an alternative way to finger the guilty microbe.

Whipple's disease is a rare bacterial infection, where the causal organism has never been isolated. The disease itself has a collection of symptoms, centred around malabsorption of certain nutrients. Symptoms, such as diarrhoea, intestinal bleeding, abdominal bloating and cramps, weight loss, arthritis and fever can continue for years until the true cause is recognized. It can be cured with antibiotics, but is usually fatal if left untreated. The range of symptoms has led doctors to think that there might well be several strains of the bacterium, but without bacterial cultures the evidence is almost pure speculation.

Researchers at the University of Zurich have used several molecular biological methods to look for bacterial DNA in tissue samples from patients with symptoms of Whipple's disease. They found some from an unknown species, which they could classify as a member of the actinomycetes. Their recent work has looked at samples from 28 patients to see if there really are several varieties of this new species, provisionally called *Tropheryma whippelii*. Their analyses revealed three types, differing at specific points in a short region of DNA. In addition, they checked on two side issues by detecting only one type in each person, even when they examined several different biopsies, and were unable to detect infection with any other bacteria in the patients.

The big question from the group's results is whether their very small, but consistent, changes in DNA sequence are real evidence for strains of *T. whippelii* which are sufficiently different to cause the variety of symptoms seen in patients. At present, the only way to answer this conclusively requires a large sample of bacterial cells, so it is back to the nineteenth century quest to grow disease causing agents in culture.

H.P. Hinrikson *et al.* Detection of three different types of *'Tropheryma whippelii'* directly from clinical specimens by sequencing, single-strand conformation polymorphism (SSCP) analysis and type-specific PCR of their 16S–23S ribosomal intergenic spacer region. *Int J Syst Bacteriol* 49, 1701–1706.



Trouble in paradise

Events in human history have left their mark on our diseases. One tragic episode in South America in the nineteenth century was probably the origin of unexpected results in a survey of the virus that can cause T-cell leukaemia, and other cancerous conditions, in adults. This virus, human T-cell leukaemia virus type I (HTLV-I), is only transmitted between people after close and frequent contact, such as during a long-term sexual relationship or breast-feeding. It is most prevalent in Africa and the continents surrounding the Pacific Ocean, although it now exists in most parts of the world. Distinctive types of the virus are found in Melanesia, Japan and South America, but the Pacific islands of Micronesia and Polynesia are surprisingly free of it.

A collaborative Japanese/Chilean survey of HTLV-I in Chile included an excursion to Easter Island, the Polynesian island closest to the South American mainland. They collected blood samples from 138 of its inhabitants and tested them for the virus. Only one person was infected, a 58-year-old woman of the Rapa Nui, the indigenous inhabitants of the island. The strain of virus was similar to ones found in South America, rather than Melanesia.

This is rather puzzling since, despite the voyage of Thor Heyerdahl on *Kon-Tiki* in the 1940s, there is now a consensus that the Rapa Nui came to Easter Island about 400 A.D. from Polynesia. However, contact between the island and the mainland in recent centuries has been far from beneficial. For example, in the nineteenth century Peruvian slavers carried away almost all of the island's men, and when some returned they brought a lethal epidemic of smallpox with them. After Easter Island was annexed by Chile in 1888 many people migrated there from South America. Indeed, blood-typing of the HTLV-I infected woman showed that she was of mixed Amerindian and Maori ancestry. The source of the virus is therefore much more likely to be South America from recent contact, rather than from Melanesia centuries ago.

■ **S. Ohkura *et al.*** Identification and phylogenetic characterization of a human T-cell leukaemia virus type I isolate from a native inhabitant (Rapa Nui) of Easter Island. *J Gen Virol* **80**, 1995–2001.

Microbial diversity in the guts of Australian mammals

There is currently much debate about the nature of bacterial species. After all, most bacterial cells have such an undistinguished appearance that microbiologists resorted to biochemical and genetic characteristics for identification purposes decades ago. This accumulation of knowledge is throwing up evidence of bacterial species with the same biochemical characteristics despite extensive rearrangements to their genetic structure.

Resolving these contradictions will require detailed analysis of bacteria from similar ecological situations. Microbiologists have always concentrated on bacteria from humans and domestic animals. As a consequence, the *Enterobacteriaceae*, a family of commensal bacteria from the gastrointestinal tract, are probably the best characterized group. The gut provides a broadly similar home, but to really delve into ecology, a wider range of hosts and geographical situations is needed.

This is where Australia comes into its own. All three living groups of mammals are found there. The platypuses and echidnas are mammals, despite laying eggs, and are the only surviving monotremes. In addition there are many species of marsupial mammals, distinguished by carrying their young in a pouch. The third group of mammals are the eutherians, which includes humans and other species introduced to Australia. However, there are native eutherian mammals in Australia, which belong to the bat and rodent families, which provide a better comparison with its other indigenous mammals. In addition to the evolutionary distance between these three groups, individual mammal families have very different diets. Some are omnivorous, others eat exclusively leaves, or pollen and nectar. Still other groups are carnivorous.

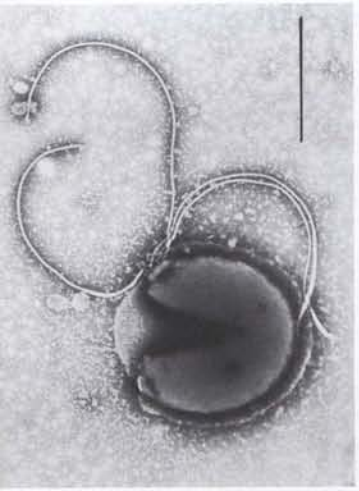
David Gordon and his colleagues Frances FitzGibbon and Joannah Lee at the Australian National University in Canberra have been examining the flora from a broad range of hosts and localities. They have worked for over 5 years with field scientists to build up a collection of 951 bacterial isolates from the fresh dung of more than 600 individual mammals, representing 79 species from 16 families. They used well known methods to isolate and identify *Enterobacteriaceae* species. Almost half the bacteria turned out to be isolates of *Escherichia coli*, which is usually accepted as the most common member of the aerobic gut flora of warm-blooded vertebrates. However, the other bacteria were isolates of another 23 species, along with a small number which could not be identified and probably represent several brand new species.

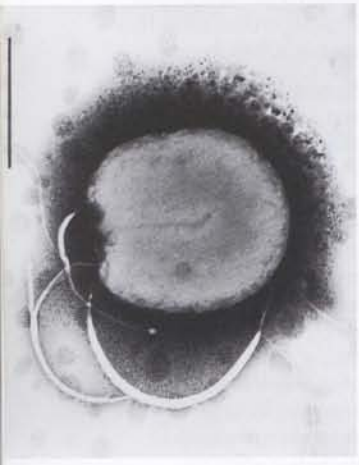
To make sense of this large amount of data, the researchers decided to apply statistical methods to relate the number of bacterial species in a particular host to mammal families and Australian states. They concluded that the mean number of bacterial species varied significantly among mammal families, and also with geographical location. Mammalian hosts from the state of Queensland and the Northern Territory had a more diverse bacterial flora than those from other states. The family of marsupial ringtailed possums and gliders (*Petauridae*) and the eutherian mammal group of bats (*Vespertilionidae*) contained a conspicuously diverse collection of enteric bacteria while the wallabies and kangaroos (*Macropodidae*) and the solitary brushtail possums (*Phalangeridae*) yielded few species in their droppings.

Some mammal families had particularly distinctive bacteria in their droppings. For example, the insect-eating bats, had *Klebsiella oxytoca* more frequently than any other group. This species of *Klebsiella* is often found in insects and may simply be passing through the bat's guts. The nature of an animal's diet is an important factor in determining the kinds of bacteria to which it is exposed. However, the results of these studies also suggest that bacteria may be adapted to the specific environments found within different kinds of mammals and to the climatic conditions where these animals live. Bacteria living in a gut have to survive in this environment as well as in the animals droppings if they are to be eaten and so return to the gut.

D.M. Gordon & F. FitzGibbon. The distribution of enteric bacteria from Australian mammals: host and geographical effects. *Microbiology* 145, 2663–2671.

D.M. Gordon & J. Lee. The genetic structure of enteric bacteria from Australian mammals. *Microbiology* 145, 2673–2682.





ABOVE:
Electron micrographs of negatively stained preparations of *Helicobacter pylori* in the decline phase of growth, illustrating early (upper) and late (lower) stages in the genesis of coccoidal forms of the bacterium. Bars, 500 µm.
COURTESY M. WORKU, IMPERIAL COLLEGE SCHOOL OF MEDICINE AT ST MARY'S, LONDON

Secrets of pathogenicity

The few bacteria that cause disease attract much more attention than the vast majority which are positively beneficial, or at least harmless inhabitants of this planet. But what characteristics do bacteria need to be pathogens? Sometimes the answer is not always obvious.

For example, some bacteria only cause infections some of the time. It is perfectly normal for coagulase-negative staphylococci to live on human skin and they occasionally cause clinical infections. One species, *Staphylococcus caprae*, has been detected infecting some people after surgery to repair or replace damaged bones. Researchers at the National Reference Centre for Staphylococci in France have been testing strains of *S. caprae* to see how these pathogenic isolates differ from ones obtained from their normal habitat, namely goat's milk.

The outcome was that their tests on *S. caprae* strains could not distinguish those isolated from infections from those isolated from goat's milk. In addition, all the strains had the capacity to produce the sort of proteins and slimy polysaccharides that are known to enhance pathogenicity in bacteria. The clinical isolates had all survived the antibiotics given to the patients to try to clear their infections, and the slime might have protected them. However, since the capacity to synthesize this slime is also present in the apparently harmless strains, the situation is obviously not one where slime production equals pathogenicity.

While an understanding of how the benign *S. caprae* can occasionally turn vicious is obviously at an early stage, much more is known about some pathogens. For example, *Haemophilus influenzae* type b regularly causes infections in both the upper and lower respiratory tract as well as occasionally launching into an invasive disease that can result in meningitis. One reason for its success is its complex lipopolysaccharide (LPS) coating. Genes involved in its synthesis, along with several others, all contain a feature which encourages the bacterial cell to make an occasional mistake and so create a new coating. Since the LPS is the way the bacteria evade the host's immune system, being able to suddenly change its coat is a distinct advantage for this pathogen.

Researchers at the University of Manchester have been looking at how changes in these genes affect the way *H. influenzae* colonizes animals. They inoculated baby rats in their noses or abdomens with one strain of *H. influenzae* and then looked for the bacteria in samples of blood, cerebrospinal fluid (CSF) and nasal washings 2 days later. They were particularly interested to see if there had been any changes to two genes involved in LPS production or to a third one which has a similar structure but an unknown role.

One of the two genes required for LPS production was unaffected by finding itself in a rat's nose instead of a laboratory culture. However, new variants of the other one had started to appear, while the third gene was almost entirely replaced by a new and functional version.

After injecting the bacteria into the rats' abdomens, the results were different. Several new versions of the genes appeared, sometimes different ones in CSF and blood from the same animal. This time it was the other LPS gene that turned out to be important, with new functional variants predominating. The implication from these results is that different versions of the LPS are advantageous to bacteria colonizing different sites in the body.

One further aspect of the success of a bacterial pathogen can be its ability to move or change shape. *Helicobacter pylori*, after some controversy, is now recognized as the major cause of peptic ulcers and non-autoimmune gastritis, as well as being a factor in gastric carcinoma. Its cells are helical in shape and move by twirling their flagella. However, non-moving, spherical cells can appear in old laboratory cultures and have occasionally been seen in samples from patients. The importance of this change has been debated but researchers at the Imperial College School of Medicine and from the University of Westminster have now worked out the relationship between these two forms.

They grew *H. pylori* in both batch culture, where the cells gradually ran out of nutrients, and in a continuous culture system, where they could keep the cells constantly supplied with any level of nutrients they chose. As the cultures grew, the scientists took out cells to monitor their motility and shape with a computerized image analysis system and an electron microscope. It soon became apparent that the bacteria moved around vigorously when growing rapidly. The cells themselves were helical, but when nutrients started to run out they gradually became spherical and stopped moving because they had lost their flagella. When the researchers looked at *H. pylori* cells in biopsies, they could see helical cells within the mucus close to the stomach surface. Their results confirm the idea that motility is an important ability for all strains of *H. pylori* that colonize a stomach. This, along with their helical shape, implies that the bacteria are constantly growing, fed by plasma exuding from the damaged stomach tissues. Any non-motile spherical cells will be rapidly removed from the stomach and might have a role in transmitting the bacteria to a new host.

J. Allegnet *et al.* Tracking adhesion factors in *Staphylococcus caprae* strains responsible for human bone infections following implantation of orthopaedic material. *Microbiology* 145, 2033–2042.

S.L. Hosking *et al.* Phase variation of *lic1A*, *lic2A* and *lic3A* in colonization of the nasopharynx, bloodstream and cerebrospinal fluid by *Haemophilus influenzae* type b. *Microbiology* 145, 3005–3011.

M.L. Worku *et al.* The relationship between *Helicobacter pylori* motility, morphology and phase of growth: implications for gastric colonization and pathology. *Microbiology* 145, 2803–2811.

JGV USA

Journal of General Virology (JGV) has appointed its first Editor in the United States. Dr John P. Moore works at The Aaron Diamond AIDS Research Center, New York, on human immunodeficiency virus (HIV), focussing especially on the envelope glycoproteins.

In addition to boosting the expertise of JGV in this crucial area the appointment of John Moore gives the Journal a vital Editorial presence in the States and an insight into current trends there.

Originally from Liverpool, UK, John studied biochemistry at Cambridge University, where he went on to do a PhD on activation of T-lymphocyte growth. After postdoctoral research in the same subject, he transferred his attention to HIV and worked on the British AIDS Vaccine Project. Following stints in Glasgow and London, John moved to New York in 1992.

New submissions to JGV on human retroviruses should be sent to:

John Moore
The Aaron Diamond AIDS Research Centre
455 First Avenue
7th Floor
New York, NY 10016
USA

Fax +1 212 725 1126
e-mail John.Moore@adarc.org

Highwire Update – Full text HTML now available for JGV

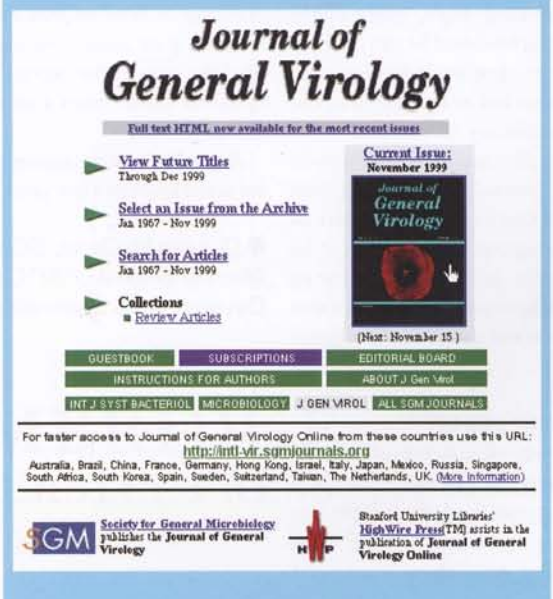
Visitors to the on-line versions of the SGM journals will know that since the sites went 'live' at the end of May, they have contained header information (title, authors, abstracts, etc.) and full text PDF files for each article, as well as useful features such as tables of contents of forthcoming issues. Work has been going on in collaboration with our printers, Cambridge University Press, on bringing the full text SGML of articles to a form fit for conversion to full text HTML at HighWire. This has involved a number of upgrades to programs at CUP and automation of several tasks previously done manually.

SGML for three complete issues of JGV was run through the 'integrity testing' procedure at HighWire and referred back to CUP for further modification. When it was judged to have reached a state of publishable quality, we were able to show the green light for it to go into production. On 18 October, the JGV site went live with full text HTML for the current (November) issue and for October, September and August as well. Further back content to January 1999 will be added as issues are processed.

The full text HTML articles offer a number of features and functions not available in the PDF versions, including inter-journal linking and enhanced searching facilities. PDFs are available in parallel for those wishing to print off a paper version.

HighWire have now started integrity testing of entire issues of *Microbiology* and a report on the first one through is eagerly awaited. It is hoped that the experience gained in bringing the JGV SGML to publishable quality will ensure that *Microbiology* will go through this phase at a faster pace, although it will undoubtedly have a few features of its own to iron out. And then we will get on with *International Journal of Systematic Bacteriology*. It is a busy time!

● *Ron Fraser, Executive Secretary*



Reviews in *Microbiology* – less is more

Since its launch in 1994, *Microbiology* has published many lively and informative Reviews. These have provided an excellent resource for those engaged in microbiological research and teaching. In response to comments from readers and suggestions by the Editorial Board, the Editors have decided to build on the success of this section by establishing a new Mini-reviews series to highlight topics of breaking interest. Paul Rainey (University of Oxford) has recently been appointed as Reviews Editor for *Microbiology* and he will be responsible for establishing this new series. He will also co-ordinate the commissioning of regular full-length Reviews, which was formerly done by the Editor-in-Chief.

Microbiology aims in the future to publish at least one Mini-review, plus, if possible, a full-length review, per monthly issue. The Reviews and Mini-reviews will cover the broadest possible range of topics of current interest.

The Reviews Editor will commission Reviews and Mini-reviews on subjects considered of importance and wide interest by the Editors and Editorial Board of *Microbiology*. However, unsolicited proposals for Reviews and Mini-Reviews are always welcomed: authors are advised to send their proposal before submitting a manuscript. Authors should bear in mind that *Microbiology* attracts a wide range of readers who are not necessarily specialists, and should pitch their text accordingly, providing enough background information to place the topic in the broader context of microbiology.

All Reviews and Mini-reviews submitted to *Microbiology*, whether commissioned or unsolicited, will be subject to rigorous independent peer review.

Those with concepts for Reviews or Mini-reviews should contact:

Paul Rainey
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UK

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● *Jon Saunders, Microbiology Editor-in-Chief*

Publishing in journals – who, why, what, where...?

Duncan McGarva

Most readers of *Microbiology Today* I suspect write and publish scientific articles or aspire to do so. We have certainly all read one or two of the items formerly known as papers. Yet hearsay, myths, rumours and speculation abound regarding authors' needs and concerns about the path to publication.

Late in 1998 the Association of Learned and Professional Society Publishers (ALPSP) decided it was timely to find out what contributors to learned journals really think about the factors involved in publishing articles. A major survey was commissioned and the detailed results have now been published – *What Authors Want*.

Four main areas were covered:

- What, at the end of the century, motivates authors to publish their work?
- How do authors decide where to publish their work?
- What concerns do authors have about the publishing process?
- What are their hopes and expectations for the future of the journal publishing process?

Questionnaires were sent out (at vast expense) by the staff of 109 journals – including the SGM's – from 38 large and small publishers, in both the scientific and arts fields. In all, 10,970 authors worldwide were contacted and an amazing 29.3% responded; 463 of the forms were completed online.

Why publish?

Regardless of the respondent's age, career stage, subject area or geographical location, communication with their peers came first, then career advancement, personal prestige and funding. Hardly anyone published for direct financial reward.

Where to publish?

The respondents considered communication to the widest possible audience and the perceived reputation of the journal to be most important; the other main factors determining journal choice were the impact factor (despite all statistical faults), the quality of peer review and the retrievability of articles by abstracting and indexing services. Also ranking high, particularly among the scientists, were presentational factors (quality of reproduction, use of colour, typeface, photographic quality). The arts authors were not as interested as the scientists in electronic availability of the journal or the ability to submit articles electronically. Authors do not care much where the journal is published, nor the nature of the publisher (society/not-for-profit or multi-megabuck commercial operation) or – if it can be found – the journal's circulation, just so long as it has an international reach. Not having to pay page charges met with approval in some quarters and the good old offprint continues to win favour.

What's happening to my paper?

Three issues arose as matters of concern about the publishing process: copyright, peer review and publication delays. Perhaps surprisingly copyright was not seen as a hindrance to publication; indeed most authors claim to understand publishers' copyright policies. When explicitly asked who should hold copyright in journal articles there was a range of opinion, the arts authors being much more strongly in favour of retaining copyright and limiting the rights the publisher is granted. (One might wonder whether this response was the result of posing leading questions the authors had not thought about before.)

Authors, editors, publishers and readers are all concerned with speed of publication. The science authors were most concerned that others would publish similar work before their article appeared; in contrast the arts group worried more about delays meaning their work was out-of-date on publication. Scientific publication might sometimes seem slow but publishing in the arts generally takes considerably longer.

Respondents seemed reasonably happy with the peer review process as it currently operates. Faults were identified, however: delay by the reviewer was the major concern; superficial or unnecessarily hostile refereeing also ranked high. When asked how the author felt when acting as a reviewer, most seemed happy with the status quo. But the matter of payment will become a more significant issue in the future.

What does the future hold?

Almost 70% of authors were of the view that scholarly publishing should continue in much its present form, though the expectation is that electronic publishing with a rapid peer review system will increase in importance. Although few authors find the options desirable, there is a perception that posting to preprint databases and electronic publication with no peer review will become more prevalent.

So what is the purpose of scholarly publishing today? Most (53 versus 34%) authors agreed with the 'contentious and portentous' statement that [it] *is changing its function from knowledge dissemination to the building of an author's résumé/CV or reputation*. Can this be right, or just the expression of the authors' personal opinions rather than a reflection of the true state of things?

And what will the answers be when the same questions are asked again in a few years' time?

Duncan McGarva, SGM Systems Manager and Member of the ALPSP Copyright and Electronic Developments Committees

For further information

Details of the report *What Authors Want*, including ordering information can be found on the ALPSP website (www.alpsp.org.uk) or can be obtained from John Morris, South House, The Street, Clapham, Worthing, West Sussex BN13 3UU, UK (Fax +44 1903 871457).

Gradline

Student Membership

Student Membership of the Society is available to postgraduate students worldwide who have no taxable income. For an annual subscription of only UK£20 (US$33) Student Members can take advantage of the many benefits that this category of membership provides, such as free registration at SGM meetings and the purchase of Society publications at greatly discounted prices.
In addition Student Members who are resident and registered for a higher degree in any European Union country may apply for awards from the President's Fund and Postgraduate Conference grants (see p. 177 for details) which provide financial assistance for attendance at scientific meetings.

Undergraduate Membership

A new category of Undergraduate Membership has recently been introduced. See p. 178 for details.

Student Societies

SGM sponsored lecture scheme

Grants are available to support **two** lectures on microbiological topics per academic year at Student Society meetings.

A Student Society is eligible for support if:

- It is run mainly by and for students of life sciences, either postgraduates and/or undergraduates.
- It is based in the UK or Republic of Ireland

The invited speakers will be reimbursed directly for reasonable costs of travel and accommodation. However, please note:

- The maximum claim for each lecture is £150.
- One speaker may be invited from abroad or from Ireland, but there can be no increase in the maximum claim for the lecture.

The Society will be reimbursed for the costs of entertaining the speaker to dinner, including the expenses of **one** member of the committee.

Application forms are available from the Grants Office at SGM HQ
Tel. 0118 988 1821
Fax 0118 988 5656
e-mail: grants@socgenmicrobiol.org.uk

Promega Prize competition 1999

University of Leeds, September 1999

On 7 September, in a hot lecture theatre at Leeds University, nine young microbiologists gathered for the final round of the Promega Prize Competition. Their presentations at previous SGM meetings had earned them a place in the final where they were required to give a 10 minute talk followed by 5 minutes of questions. Pat Goodwin, SGM Scientific Meetings Officer, chaired the session and the contestants were as follows.

- **Olivia McAuliffe** University College Cork
  Lacticin 3147: a bacteriocin with applications in food and medicine
- **Susan Lynch** University College Dublin
  The genetic analysis of amphotericin B biosynthesis
- **Jyoti Velayudhan** University of Sheffield
  The crucial role of a ferrous iron uptake system in iron acquisition and virulence in the human gastric pathogen Helicobacter pylori
- **Catriona Kydd** University of Bath
  A novel aldolase from the hyperthermic archaeon Sulfolobus solfataricus
- **Holly Slater** John Innes Centre, Norwich
  A specialized two-component system links cell–cell signalling to pathogenicity gene expression in Xanthomonas campestris
- **Gina Manning** Central Veterinary Laboratory, Surrey
  Identification and characterization of Campylobacter jejuni genes involved in host cell invasion
- **Karen Isherwood** CBD Porton Down
  Quorum sensing in Yersinia pestis
- **Gulnur Coskuner** University of Newcastle
  Distribution of ammonia-oxidizing bacteria in activated sludge flocs characterized by FISH (fluorescence in situ hybridization) technique
- **Ian Goodfellow** University of Glasgow
  Inhibition of echovirus entry into rhabdomyosarcoma cells by antiserum to cd59: a common cell-specific entry mechanism for echoviruses?

All entrants gave fluent presentations using excellent visual aids and dealt with some tough questions. The judges were Group representatives Peter Andrew, Eric Blair, Martin Collins, Reg England, Dave Hodgson, Keith Jones, Mike Wilson and Peter Wynn-Jones, with Pat Goodwin in the chair and Kiran Ghanaker representing Promega. Although the overall standard was high, two entrants stood out as winners: **Gina Manning** and **Karen Isherwood** who both took the time to put their work in a wider perspective and whose talks were particularly accessible to a non-specialist.

The names of the winners were announced at the Young Members' Reception that evening and each have received a cheque for £200. Since the standard of competition was so high, the judges felt that all runners-up should receive a prize of a year's free membership of the SGM.

Gina and Karen will go on to represent the Society for the *Promega Young UK Life Scientist of the Year* Award which will be held in 2000. There they will be competing against other Promega prize winners from the Biochemical Society, the Genetical Society and the British Society for Immunology for a prize of £2,000 and a trophy.

If you are a postgrad or postdoc under 28, why not enter the SGM Promega Prize competition next year. All you need to do is present a poster or an oral offered paper at a Society meeting and let the Meetings Office know that you wish to be considered. See the website for details.

Young Members' Reception
University of Leeds, September 1999

CVs and interviews

Alan Garmonsway, a human resource specialist for Xenova Group, shared his expertise on job-hunting in the biosciences in an entertaining and eye-opening talk. A panel of individuals from different job sectors then fielded a barrage of questions from the floor. Pat Goodwin from the Wellcome Trust, Liz Sockett (SGM Education Officer and academic at Nottingham University) Kiran Ghanaker (a product application specialist at Promega) and Katrina Halliday of Cambridge University Press were all able to share their knowledge and experience with young members of the Society.

Alan's presentation began with a brief introduction to new-speak in industry, a description of how working practices have changed in recent years and how this affects scientists employed there. Job applicants must now adapt to meet these changes and can no longer expect to find a job for life. A summary of the recruitment process revealed that approximately 80% of job applicants de-select themselves before shortlisting even begins. This can happen for a variety of reasons, including an unreadable letter or CV, or lack of adequate information in the application. Alan then spent some time showing how to write an application that makes it through the selection process to interview. Each step of the application was considered: from how to read the advert from the recruiter's point of view to how to organize information to your best advantage. He illustrated his talk with some entertaining 'disasters' that have passed through his office.

Alan next considered the interview process. He outlined how to communicate the type of information that interviewers aim to discover about applicants and listed some useful 'do's and don'ts' for that all important day. He continued his talk with a reminder of the different approaches to finding that elusive job, including networking at meetings, responding to adverts and moving from temporary to permanent employment (not uncommon in industry). To finish, Alan summarized with some useful key points for successful job hunting.

The lively question and answer session which followed Alan's excellent talk only ended at the promise of a delicious buffet and glass or two of wine. All panel experts stayed to answer individual questions during the meal and discussions lasted well into the evening.

If you would like a factsheet on *CVs and Interviews*, based on Alan's talk, please contact Jane Westwell at SGM HQ:
Fax 0118 988 5656
e-mail careers@socgenmicrobiol.org.uk

Further careers information is available on the SGM website at http://www.socgenmicrobiol.org.uk.

Careers factsheets

Graduate careers factsheets on the web

Jane Westwell of the External Relations Office has created some factsheets on careers for graduate microbiologists. These cover the following topics:

- *Careers Information for Graduate Microbiologists*
- *Careers Out of the Laboratory*
- *Research Careers for Postdoctoral Microbiologists*
- *Careers in Environmental Microbiology*
- *Careers in Medical Microbiology*

These are all available as downloadable PDF files on the SGM website (www.socgenmicrobiol.org.uk)

Click on the 'Careers and Education' button and follow the links.

● Contributions for Gradline from young SGM members are always welcome.

WFCC Skerman Award for Microbial Taxonomy

The World Federation for Culture Collections invites applications from young microbial taxonomists for the WFCC Skerman Award for Taxonomy. The Award was established to honour the contribution made by Professor V.B.D. Skerman to bacterial taxonomy, to the establishment of the WFCC World Data Centre on Microorganisms and to the development of the WFCC.

The aim of the Award is to encourage taxonomic research by young microbiologists and to reward excellence in taxonomic research and significant contributions to the discipline.

The successful recipient of the Award will receive a prize of US$2,000 together with a return economy class airfare and registration costs to attend the Ninth International Congress for Culture Collections to be held in Brisbane, Australia, during the period 23–28 July, 2000, and will be invited to deliver the Skerman Award Lecture on their research. The recipient will also receive a certificate of the Award.

Applicants should normally be less than 40 years of age at the time of application. Applicants should provide a CV, a list of research publications, the names and addresses of two referees familiar with their research who have agreed to act as referees and copies of their three most significant research publications. Applications should be submitted to:

Dr Alan Doyle, WFCC Secretary
The Wellcome Trust
183 Euston Road
London NW1 2BE, UK
Tel. +44 171 611 8248
Fax +44 171 611 7277
e-mail a.doyle@wellcome.ac.uk

The closing date for applications is 31 December 1999.

Reviews

If you would like your name to be added to our database of book reviewers, please complete the book reviewer interests form now available on the SGM website. A classified compendium of book reviews from 1996 to the present is also available on the website.

Introduction to Bioinformatics. Cell and Molecular Biology in Action Series

By T.K. Attwood & D.J. Parry-Smith
Published by Addison Wesley Longman (1999)
£17.99, pp. 218
ISBN: 0-582-32788-1

For the purposes of this book, bioinformatics means molecular sequence and structural information, which is probably what most people would assume anyway. It does not address broader issues of data linkage or molecular structural analysis but concentrates on sequence analysis, drawing on structural information where appropriate. The book is ideally suited to student teaching, although it is an excellent primer for anyone still on the fringes of the molecular revolution. Interestingly, it is accompanied by a splendid web site <http://www.bioinf.man.ac.uk/dbbrowser/bioactivity/prefacefrm.html> containing a practical exercise to reinforce the material presented in the book. The only drawback with the book is that, in such a fast-moving field, some of the references and internet sites are now either out-of-date or incomplete. Nonetheless, this is a super book which is highly recommended, but use it soon while it is still fresh.

■ ***Dave Roberts***
The Natural History Museum, London

The Cytokine Handbook Third Edition

Edited by A.W. Thomson
Published by Academic Press (1998)
£85.00, pp. 1017
ISBN: 0-12-689662-3

The complexity of the cytokine field has increased exponentially, and so have the books in this area! *The Cytokine Handbook* succeeds in covering a large percentage of this field so central to immunology. The book covers all interleukins up to IL-18, chemokines and their receptors, as well as TNF, TGF-β, GMCSF, and Flt3-L, among others. Four out of the 32 chapters cover specific therapeutic applications, including gene therapy. The book thus provides in-depth overviews of current research, including updated discussions on the basic molecular biology and clinical applications of each cytokine. Detailed tables throughout make it easy to scan the plethora of activities displayed by individual cytokines across tissues, organs and species. Thus, this is an excellent guide to the novice to find a way into the cytokine maze, or for the experienced researcher to become updated.

■ ***Pedro R. Lowenstein***
University of Manchester

Sexually Transmitted Infections and Aids in the Tropics

Edited by O.P. Arya & C.A. Hart
Published by CABI Publishing (1998)
£60.00/US$110.00, pp. 448
ISBN: 0-85199-262-5

Chilling statistics confront all those involved in the global fight against HIV and AIDS. The focus on sexually transmitted disease in the tropics (here concentrating mainly on Africa) is appropriate. A recent trip to South Africa has confirmed first-hand the role STD played in the HIV epidemic. This book contains up-to-date statistical information and good relevant references. There is a balanced contribution from experts working in the front line. Helpful illustrations, practical tips, tables and algorithms add to the comprehensive discussion of STD. The structure of the book is excellent. Introductory chapters set the broad scene and describe epidemiology, anatomy and immunology of the genital tract. This is not a book to be read at bedtime. It is a text which will be an indispensable addition to a departmental library, a necessary book for HIV clinicians and a useful reference book for those who teach in this field.

■ ***Sheila M. Burns***
Regional Clinical Virology Laboratory, City Hospital, Edinburgh

Rapid Detection of Infectious Agents. Infectious Agents and Pathogenesis Series

Edited by S. Specter, M. Bendinelli & H. Friedman
Published by Plenum Press (1998)
US$69.50, pp. 245
ISBN: 0-306-45848-9

This volume contains several interesting and informative chapters on aspects of laboratory diagnosis of human pathogens. The chapters by diverse authors are united by consideration of different analytical techniques and their application to diagnostic problems, but vary considerably in style and content, ranging from protocols to reviews. Human viruses and some pathogenic bacteria are most thoroughly considered with little or no mention of fungi or parasitic organisms. The section on genetically engineered cells in diagnostic virology was a particularly useful summary of an area which is beginning to filter into commercial practice. Nevertheless, there were some notable omissions, including Amplified Fragment Length Polymorphism, near patient tests and some of the more recent improvements in enzymology of direct PCR detection of pathogens. Surprisingly also, the justification for the term 'rapid diagnosis' was not always evident in the sections included. Despite these shortcomings, the book is highly recommended for individuals with an interest in diagnostic virology/bacteriology and institutes or departments containing diagnostic laboratories.

■ ***Maria Zambon***
Virus Reference Division, CPHL, London

Biotherapeutic Agents and Infectious Diseases

Edited by G.W. Elmer, L.V. McFarland & C.M. Surawicz
Published by Humana Press (1998)
US$125.00
ISBN: 0-89603-647-2

Biotherapeutic agents – this is a term for what many would call probiotics, a topic often relegated to alternative medicine. One senses a determined attempt by the Editors to legitimize the area. The introductory chapter gives an excellent account of the QC and regulatory issues involved in getting a product licensed, but is totally parochial, with no mention of the requirements for regulatory bodies other than the FDA. Other chapters cover various diseases, including cystitis, antibiotic-associated diarrhoea, vaginitis and *Clostridium difficile*-associated disease, and each gives a good review of the studies to date on the use of probiotics. I felt that too much space is taken up describing the disease, a topic that is covered in many other books. Most chapters point out the need for double-blind, placebo-controlled studies, and suggest ways forward in assessing these agents. Although there is much to recommend this book, some chapters can be rather turgid, and the high price may well dissuade many.

■ ***Pam Hunter***
Burnthouse, Burnthouse Lane, Cowfold, Sussex

Diagnostic Virology Protocols. Methods in Molecular Medicine, Vol. 12

Edited by J.R. Stephenson & A. Warnes
Published by Humana Press (1998)
US$79.50, pp. 384
ISBN: 0-89603-401-1

As a clinical virologist my expectation of diagnostic protocols turned out to be different from that of the Editors. I was expecting a symptomatic or systematic approach to the diagnosis of virus infection, i.e. likely organisms, types of specimens required, investigation strategies and some information on how these investigations would affect patient management. The protocols described in this book are the bench level investigations that one might carry out after deciding which group of infecting organisms to study.
The book is full of PCR protocols described in greater detail than is

normally possible in journal publications; the authors of each chapter have shared many of the trade secrets that make the difference between success and failure. The Editors have also required that each author end their chapter with a section of further advice notes; the enterovirus and parvovirus chapters were particularly well done in this respect. A useful book for a short period of time as I suspect that many of those methods will have been adapted further in the meantime. However it does present a list of recognized experts in their fields for those interested to contact directly.

■ ***Liz Boxall***
PHL, Birmingham Heartlands Hospital

The Microsporidia and Microsporidiosis

Edited by M. Wittner & L.M. Weiss
Published by ASM Press (1999)
£73.00, pp. 553
ISBN: 1-55581-147-7

What a timely book! Microsporidia have attracted a lot of interest as parasites and more recently as model organisms in molecular evolution. This up-to-date compilation on microsporidia biology – typically scattered among protozoological, parasitological/medical and evolutionary journals – is a must. Each chapter (most are well written) gives detailed descriptions of microsporidia biology, such as ultrastructure, biochemistry, molecular biology, culture and epidemiology, is nicely illustrated, well referenced and indexed. There is a useful glossary and several chapters present protocols for microsporidia identification. It sets the scene for years to come during which molecular cell biology and biochemistry will bring much needed discoveries on the functioning of the microsporidia.
A must-get book for students, biologists and medical doctors interested in molecular cell biology, parasitology or evolutionary biology. If you work on microsporidia *per se* why don't you have it already? If you do not buy it, ask your library!

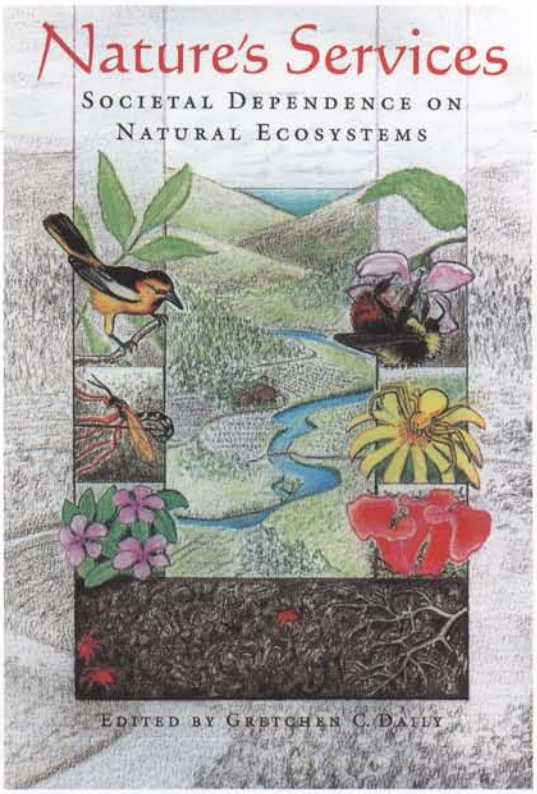
■ ***Robert Hirt***
The Natural History Museum, London

Protein Synthesis: Methods and Protocols. Methods in Molecular Biology, Vol. 77

Edited by R. Martin
Published by Humana Press (1998)
US$74.50, pp. 400
ISBN: 0-89603-397-X

As one would expect, a book of methods and protocols in molecular biology is pretty much a 'cookery book' but necessary nonetheless. This volume in the popular *Methods in Molecular Biology* series contains 29 chapters by 65 international contributors. Each chapter starts with a concise, informative and well-referenced introduction before listing materials (including leading suppliers) and methods. The methods are helpfully detailed and carry the feel of being written by those who have actually carried out these experiments and know what step is or isn't crucial. For example, in the section on *Xenopus laevis* translational activity there are extensive notes outlining potential problems, i.e. '*In our hands, a major problem in working with both egg and oocyte extracts is the loss of translational activity exhibited when the extracts are frozen and thawed... even when great care is taken to freeze the sample rapidly...*' (p. 205). This can be very comforting to the poor postgrad or postdoc at the bench given the task of repeating others' protocols and is invaluable for showing to disbelieving supervisors! Overall an excellent, detailed protocols book, a copy of which should be on the shelves of every molecular biology lab.

■ ***Janet Bunker***
SGM Education Group Committee



Nature's Services. Societal Dependence on Natural Ecosystems

Edited by G.C. Daily
Published by Island Press (1997)
£19.95, pp. 392
ISBN: 1-55963-476-6

Nature's Services comprises chapters contributed by experts in a wide range of disciplines and focuses on an appreciation of societal dependence upon natural ecosystems. It attempts to look at man's potential disruption of ecosystems and its consequences. Using man as the 'consumer' in an economic sense, different ecosystems are described in terms of their ecology, their importance and how they deliver benefits to the consumer, culminating in an appreciation of how their value can be incorporated in decision-making processes. Each chapter is concise, logically structured and contains a range of references from scientific papers, books and government reports. This book would not be priority for most microbiologists, particularly as it contains little microbiological information, apart from elementary information, but it does give a different view on man, ecology and the biosphere. It is not, however, a casual reading book and it would be difficult to identify the ideal target reader.

■ ***Roger Pickup***
Institute of Freshwater Ecology, Cumbria

Biology Now! 11–14 *(1) Pupil's Book* *(2) Teacher's Resource Book*

By P.D. Riley
Published by John Murray (Publishers) Ltd (1998)
(1) £9.99; (2) £35.00
ISBN: (1) 0-7195-7548-6; (2) 0-7195-7549-4

Biology Now! 11–14 is one of a series of three pupil's books (supported by a Teacher's Resource Book) that covers both Ks3 of the National Curriculum for Science and also the Common Entrance Exam at 13+. The other titles in the series are *Chemistry Now! 11–14* and *Physics Now! 11–14*.
The book is attractively presented in full colour with many photographs and diagrams which convey information clearly and accurately. Throughout each chapter there are a variety of questions to suit a range of abilities. Some can be answered directly through reading the text, others stimulate thinking and could be used as the basis of a class discussion. Chapter summaries are provided for revision purposes. There is also a comprehensive glossary.
The classification of micro-organisms is covered in the chapter 'Looking at Living Things', whilst 'Keeping Healthy' looks at how bacteria and viruses affect health and how the body fights infections. This includes the use of antibiotics and also immunization. The Teacher's Resource contains photocopiable worksheets, many of which are practical investigations. These provide precise instructions and adequate safety information and there are clear explanations to the skills and concepts being introduced. It concludes with examples of Ks3 exam questions and a 13+ question bank.
This is a very useful text to support biology teaching across the 11–14 age range.

■ ***Dariel Burdass***
SGM, Marlborough House

HIV Protocols. Methods in Molecular Medicine, Vol. 17

Edited by N.L. Michael & J.H. Kim
Published by Humana Press (1999)
US$89.50, pp. 432
ISBN: 0-89603-369-4

This collection of laboratory techniques used in the HIV field is organized in four parts: virology, molecular biology, humoral and cellular immune responses to HIV. The strength of this manual comes from its focus on methodological details and the provision of especially valuable 'hints and tips', the description of some of the latest technology, and the inclusion of the most recent advances in HIV research. Chapters include an introduction to the technique, its role in the field and a concise list of references, including the classical papers. On the less positive side, chapters on labour-intensive techniques do not always mention the available commercial kits, studies on the primary site of HIV replication (secondary lymphoid tissues) and genotypic or phenotypic assays for the evaluation of HIV-1 drug resistance are not mentioned. This book remains of great value to labs performing basic HIV research and considering more advanced techniques.

■ ***Mounir Ait-Khaled***
GlaxoWellcome, Stevenage

Therapies for Viral Hepatitis

Edited by R.F. Schinazi, J.-P. Sommadossi & H.C. Thomas
Published by International Medical Press (1998)
£79.99 + £7 p&p UK; £8.50 p&p Europe/ US$129.00 +US$10 p&p *or* US$20 by courier; ROW US$42 surface mail; US$45 by courier
ISBN: 1-901769-01-1

The title of this book is somewhat misleading for two reasons. First, only the agents responsible for chronic hepatitis (i.e. HBV, HCV and a token mention of HDV) are considered, and second, the scope is far wider than just therapy. The 48 contributions cover a range of topics from epidemiology and pathogenesis to drug design and animal models. However, the Editors have skillfully blended the contributions so that their relevance to the overall theme of the development and application of therapeutic regimes for the control of chronic viral hepatitis is well maintained. The authorship includes many major figures in the field and the individual chapters are generally succinct and very readable. In conclusion, the book is a compilation of authoritative articles and presents a useful snapshot of the problems and prospects in chronic viral hepatitis in the late 1990s.

■ ***Dave Rowlands***
University of Leeds

Combination Vaccines: From Clinical Research to Approval

Edited by R.W. Ellis
Published by Humana Press (1999)
US$ 125.00, pp. 292
ISBN: 0-89603-717-7

The development and use of bacterial/viral combination vaccines is driven by the desire to combine an increasing number of childhood vaccines into fewer visits for inoculation. This book addresses the necessity for multivalent vaccines, the need for suitable and effective combinations, the formulation of regulatory guidelines and the logistics of achieving wide vaccine coverage.
Of particular interest are the chapters on pharmaceutical aspects of combination vaccines, on efficacy testing and on issues for health practitioners. More weight could have been given to the discussion of incorporation of new combination vaccines into the Extended Programme of Immunization (EPI) of the WHO, with particular reference to the problems of vaccine coverage in developing countries.
The book is of interest to those involved in public health. It is informative and reads well. References are comprehensive and reach well into 1998 in places. The price is on the high end but on balance worth spending.

■ ***Ulrich Desselberger***
PHL Cambridge

Hepatitis C Protocols. Methods in Molecular Medicine, Vol. 19

Edited by J.Y.-N. Lau
Published by Humana Press (1998)
US$89.50, pp. 640
ISBN: 0-89603-521-2

This book is clearly intended as a laboratory companion volume and comprises a collection of recipes and experiences from many of the foremost practitioners in HCV research. I think that it nicely fulfils an important role by providing 'nitty gritty' detail to researchers wishing to explore the application of new procedures to their work. It also, of course, lays down the challenge to the new practitioner to obtain the quality and reproducibility of results claimed by the authors. Given that the book is a laboratory manual, a loose-leafed version with the facility to add extra pages of notes would have been doubly useful. The target readership for the book is necessarily individuals and laboratories conducting HCV research, but the reasonable price and the wide range of practical information provided should make it an essential buy for this group.

■ ***Dave Rowlands***
University of Leeds

HIV and the New Viruses, Second Edition

Edited by A. Dalgleish & R. Weiss
Published by Academic Press Inc. (1999)
US$125.00, pp. 537
ISBN: 0-12-200741-7

This is a comprehensive and up-to-date volume that reviews our current knowledge of HIV and other recently identified viruses of humans. Half of the book is devoted to HIV and covers all aspects of the virus from the molecular biology of the regulatory proteins to epidemiology and antiviral therapy. The only omission is discussion of the Nef protein, surprisingly, given its importance for viral pathogenesis. Information about other new viruses tends towards epidemiological and clinical aspects, although chapters on KSHV and HBV provide some background to the molecular biology of the viruses. In general I found the chapters to be detailed and well written with a healthy supply of illustrations to aid understanding. The book will be of most use to those involved in teaching virology and should certainly be recommended to libraries as a general reference volume for both undergraduates and postgraduates.

■ ***Mark Harris***
University of Leeds

The Fungal Colony. British Mycological Society Symposium Series, Vol. 21

Edited by N.A.R. Gow, G.D. Robson & G.M. Gadd
Published for the BMS by Cambridge University Press (1999)
£65.00, pp. 332
ISBN: 0-521-62117-8

Olsson, in Chapter 2, prefers to use the term Functional Mycelium Unit rather than fungal colony but I guess *The Fungal Colony* makes for a better book title. In the Preface to the book, the Editors state their aims of covering the growth and development of fungi in natural and artificial environments, so the concept of a colony is viewed rather broadly. Any expectations of a focus on agar-grown colonies are soon dashed and the Petri dish is dismissed in the first Chapter as a sensory deprivation chamber, a theme which is warmed to in several subsequent chapters where the focus is on natural environments. Elsewhere in the book we are treated to an eclectic mix of topics, discussed by appropriate experts, that range from enzyme production in submerged cultures and regulation of hyphal branchings to sex. What unites these chapters is the hypha, that feature of filamentous fungi which holds the key to fungal lifestyles and makes this book of interest to most mycologists.

■ ***David Archer***
IFR, Norwich

Microbiology in Action: Studies in Biology

By J. Heritage, E.G.V. Evans & R.A. Killington
Published by Cambridge University Press (1999)
£12.95/ US$20.95, pp. 290
ISBN: 0-521-62912-8

This volume states that it is '*essential reading for undergraduates*' and '*of interest to sixth form students and their teachers*'. To test this I asked undergraduate David Blackley to co-review it. We find that although the book is written in a seemingly interesting question and answer style, the answers lack the depth that a first year undergraduate would want. The rather dull format and lack of illustrations would deter sixth formers from using it when web pages such as http://commtechlab.msu.edu/sites/dlc-me/zoo/ and http://www.microbeworld.org/mlc/ are more attractive. The book might be a primer for a sixth form teacher willing to research topics further for a lesson, but many of the subjects covered are not part of the high school syllabus. The companion volume to this (*Introductory Microbiology*, by the same authors), while having the same simple format, is informative and useful. Unfortunately the format doesn't work as well for the *Microbiology in Action* topics.

■ ***Liz Sockett & David Blackley***
University of Nottingham

Molecular Fungal Biology

Edited by R. Oliver & M. Schweizer
Published by Cambridge University Press (1999)
£21.95/ US$34.95, pp. 377
ISBN: 0-521-56784-X

There have been a few new mycological texts published in recent years and this is one of the best. Rather than even attempting to redress traditional texts in modern clothes, the book takes a bolder approach and wilfully omits great tracts of mycology to enable the reader to focus on what are the contemporary front lines. I think it works very well. There are only 12 carefully selected chapters in this text, almost all of which have a fresh face. Let me just highlight the chapters on fungal phylogeny, yeast genomics, metabolic flux and plant pathology as examples of summaries which step ahead of the orthodox and provide modern overviews with an appreciation of the research coal face. I am sure this book will achieve its editorial objective in informing and stimulating a new generation of up-and-coming mycologists. It deserves to be read and taken note of.

■ ***Neil A.R. Gow***
University of Aberdeen

Molecular Evolution. A Phylogenetic Approach

By R.D.M. Page & E.C. Holmes
Published by Blackwell Science (1998)
£24.95, pp. 346
ISBN: 0-86542-889-1

The process of generating a sequence for any gene will inevitably lead at some stage to the question 'how is this new sequence related to what's in the database?' Equally inevitably this

will lead some poor student (it's always a PhD student) to dip a reluctant toe into the horrific mathematical minefield of phylogenetic analysis.
Fortunately nowadays, at the click of a button (try <http://iubio.bio.indiana.edu> for starters), it is possible to download phylogenetic packages of such fearsome power that no knowledge of how they work seems to be required, indeed few of us actually understand what the results they generate mean. Faced with a log likelihood ratio of 7.36 most retreat into gross over-simplification, an attitude best summarized as 'does the tree look pretty enough to convince the referee and get this damned paper published?' Unfortunately for the poor student, the chapter in their thesis in which that tree appears is likely to generate questions like 'and what exactly is parsimony?' from their examiners. This book is intended to rescue us all from that question.
Page and Holmes explain most concepts in phylogenetic analysis in a clear and jargon-free manner without recourse to more than the most basic of arithmetic. Enough material is covered to allow the student to understand what Tajima's *D* value is for, even though they will need to rely on the computer software to calculate it (after all, that's what computers are for!). The authors begin from the basic properties of populations, such as Hardy–Weinberg equilibrium, which are equally well covered by many other textbooks, and from this familiar territory gently lead the reader through the concepts which underpin phylogenetics, explaining how evolutionary processes are thought to work and explaining clearly why there are so many different ways of calculating what seems to be the same result. The authors' focus on the underlying concepts results in a surprisingly readable book on what can be a very dry subject.
■ ***Peter Balfe***
Windeyer Institute, London

Tobacco Mosaic Virus: One Hundred Years of Contributions to Virology

Edited by K.-B.G. Scholthof, J.G. Shaw & M. Zaitlin
Published by The American Phytopathological Society (1999)
US$49.00, pp. 264
ISBN: 0-89054-236-8.

This book can be enjoyed on several levels. There are 26 classic papers to read or re-read, which illustrate the development of virology, exemplified by the study of TMV, and which also illustrate the development of the scientific paper through the century. But for me, even more enjoyable are the commentaries that accompany the papers, written by scientists who have special knowledge of the background to the work described. This is the human face of science, the effort, the insight and the sheer luck that lay behind the famous milestones. Here too the discerning reader can detect the echoes of ancient rivalries and see how narrow is the dividing line between fame and anonymity.
I heartily recommend this book to anyone with an interest in the tradition of science, and in the way the practice of virology has evolved over a hundred years.
■ ***David J Robinson***
Scottish Crop Research Institute

Easy Mathematics for Biologists

By P.C. Foster
Published by Harwood Academic Publishers (1998)
£12.95/US$18.50/EUR17.00, pp. 106
ISBN: 90-5702-339-3

This is a student workbook covering basic mathematical skills required by all biologists – the ability to handle units, concentrations, dilutions, exponents, logs, the simplest equations, straight-line graphs and the transformation of non-linear graphs into straight lines. The author has much experience of the needs and problems of biology students and usefully provides several different worked examples of each point, plus structured practice questions based on common biological problems. However, its coverage is very basic – which may well be its major attraction to students wanting to develop their skills on their own. But most tutors will need to take microbiology students a little further into equations and statistics and this otherwise excellent resource won't be enough on its own. It will overlap too much with other texts, such as David Phoenix's *Introductory Mathematics for the Life Sciences* (Taylor & Francis 1997). Perhaps the two should get together for a joint second edition.
■ ***Ron Bishop***
University of Ulster

Peptide Nucleic Acids: Protocols and Applications

Edited by P.E. Nielsen & M. Egholm
Published by Horizon Scientific Press (1999)
£59.99/US$119.99, pp. 262
ISBN: 1-898486-16-6.

The use of peptide nucleic acid is a novel and growing field. This book brings together a collection of protocols, ranging from the synthesis of PNA to its use in a number of molecular applications. The information is logically presented, with each chapter taking the form of a short publication. Although there is limited troubleshooting information, each method is presented in a clear and concise manner, together with appropriate results and discussion. However, due to the nature of the protocols, there is inevitably some overlap between chapters.
This book would be an excellent source of information for individuals who are interested in PNA technology and its relevance to their own research. It would also be useful for the researcher who was perhaps not aware of PNA, but who would like to find out more. It is perhaps less relevant for workers already in the field as it is limited to standard protocols.
■ ***Gerald Owenson***
University of Warwick

DNA Topoisomerase Protocols, Vol. 1: DNA Topology and Enzymes. Methods in Molecular Biology, Vol. 94

Edited by M.-A. Bjornsti & N. Osheroff
Published by Humana Press (1999)
US$79.50, pp. 340
ISBN: 0-89603-444-5

This volume is a highly specialized text of great value, but only to those laboratories involved in topoisomerase research or thinking about getting involved in this area. As is typical of the Humana Press *Methods* series the chapters are enhanced by the addition of 'tricks of the trade' for those new to particular techniques. With this volume, the compendium of DNA topoisomerase amino acid sequences is a nice touch. This book is essential reading for postgraduate students and technicians embarking on topoisomerase-related projects in chemotherapy, both anti-cancer and anti-microbial. I am looking forward to the publication of volume two.
■ ***Ian Morrissey***
GR Micro Ltd, London

Quantitative PCR Protocols. Methods in Molecular Medicine, Vol. 26

Edited by B. Kochanowski & U.Reischl
Published by Humana Press (1999)
US$69.50, pp. 320
ISBN: 0-89603-518-2

How refreshing, a realistic appraisal as to whether PCR can be truly quantitative. The Editors of this book rightly state that the truth lies somewhere between myth and reality. The book then goes on to deal with the theoretical considerations and some practical protocols for achieving quantitative PCR. The theoretical aspects are well covered, including some mathematics – but don't panic you don't need to understand the maths to follow the arguments. A number of chapters overlap, but this is a good thing. With no clear-cut answers to some of the problems, it is nice to see a variety of views on contentious issues. The protocol section is comprehensive and well laid out and should enable anyone to repeat these procedures. This book seems ideally suited for institutional purchase. People are going to do 'quantitative PCR' so they should look at this book and do it as best as they can.
■ ***Tony Carroll***
GlaxoWellcome R&D, Stevenage

Books Received

●Iron and Infection. Molecular, Physiological and Clinical Aspects, Second Edition
Edited by J.J. Bullen & E. Griffiths
Published by John Wiley & Sons Ltd (1999)
£120.00, pp. 515
ISBN: 0-471-93940-4

●Adhesion Protein Protocols. Methods in Molecular Biology, Vol. 96
Edited by E. Dejana & M. Corada
Published by Humana Press (1999)
US$69.50, pp. 240
ISBN: 0-89603-417-8

●Bacteria in Biology, Biotechnology and Medicine. 5th Edition
By P. Singleton
Published by John Wiley & Sons Ltd (1999)
£22.50
ISBN: 0-471-98880-4

●Biology, Fifth Edition
By N.A. Campbell, J.B. Reece & L.G. Mitchell
Published by Addison-Wesley Longman (1999)
£27.99, pp. 1175
ISBN: 0-201-52262-4

Diary

january 2000

THE DYNAMICS OF VIRUS INFECTIONS

The Royal Society, London
19–20 January 2000

CONTACT: Mr Nicholas Boross-Toby, Meetings Lectures and Awards Officer, The Royal Society, 6 Carlton House Terrace, London SW1Y 5AG (Tel. 0171 451 2574; Fax 0171 451 2693; e-mail nicholas.boross-toby@royalsoc.ac.uk; http://www.royalsoc.ac.uk)

february 2000

INTERNATIONAL COURSE IN LABORATORY METHODS FOR THE DIAGNOSIS OF LEPTOSPIROSIS

Amsterdam, The Netherlands
21–25 February 2000

CONTACT: Dr W.J. Terpstra, Royal Tropical Institute (KIT), Meibergdreef 39, 1105 AZ Amsterdam, The Netherlands (Tel. +31 20 5665454; Fax +31 20 6971841; e-mail i.struiksma@kit.nl; http://www.kit.nl)

FUNCTIONAL FOODS 2000

The Hague, The Netherlands
29 February–2 March 2000

CONTACT: Marleen Jerusalem, IPI BV, The Netherlands (Tel. +31 547 271 566; Fax +31 547 261 238; e-mail marleen@ipi-bv.nl) or Fiona Angus, Leatherhead Food Research Association, Surrey (Tel. 01372 822217; Fax 01372 822272; e-mail fangus@lfra.co.uk)

april 2000

GREEN-TECH®. INTERNATIONAL CONFERENCE AND EXHIBITION ON SUSTAINABLE AND RENEWABLE RAW MATERIALS

Royal Dutch Jaarbeurs, Utrecht, The Netherlands, 3–5 April 2000

CONTACT: Mrs Barbra Pullens, Europoint, PO Box 822, NL-3700 AV Zeist, The Netherlands (Tel. +31 30 6933489; Fax +31 30 6917394; e-mail info@europoint-bv.com; http://www.europoint-bv.com)

10TH TENOVUS-SCOTLAND SYMPOSIUM: GENE EXPRESSION AND DISEASE

Royal Scottish Academy of Music and Drama, Glasgow
10–12 April 2000

CONTACT: Dr Uta Böger-Brown, BioMedEx, 22 Allan Road, Killearn, Glasgow G63 9QE (Tel. 01360 551082; Fax 01360 551083; e-mail uta@biomedex.demon.co.uk; http://www.gla.ac.uk/Acad/IBLS/molgen/tenovus/tenovus_2000.html)

MICRO 2000

Novotel London West, London
11–13 April 2000

CONTACT: Allison Winton, Publicity Officer, Royal Microscopical Society, 37/38 St Clements, Oxford OX4 1AJ (Tel. 01865 248768; Fax 01865 791237; Conference e-mail rebecca@rms.org.uk; Exhibition e-mail allison@rms.org.uk; http://www.rms.org.uk)

NEW HORIZONS FOR PHAGE ANTIBODY DISPLAY TECHNOLOGY

Cleminson Hall, University of Hull, 11–13 April 2000

CONTACT: R.E. Green, Dept of Surgery, University of Hull, Cottingham Road, Hull HU6 7RX (Tel. 01482 466032; Fax 01482 466996; e-mail r.e.green@medschool.hull.ac.uk)

MOLECULAR BIOLOGY UPDATE. A FOUR-DAY LABORATORY COURSE

University of Hertfordshire, Hatfield, 17–20 April 2000

CONTACT: Prof. John Walker, Dept of Biosciences, University of Hertfordshire, College Lane, Hatfield, Herts AL10 9AB (Tel. 01707 284546; Fax 01707 284510; e-mail j.m.walker@herts.ac.uk; http://www.herts.ac.uk/natsci/STC)

june 2000

3RD INTERNATIONAL MEETING ON THE MOLECULAR GENETICS AND PATHOGENESIS OF THE CLOSTRIDIA

Kazusa Academic Park, Kisarazu, Chiba, Japan
8–11 June 2000

CONTACT: Rick Titball (e-mail rtitball@dera.gov.uk). For programme details, registration and abstract submission, see http://w3.ouhsc.edu/cp2000/

NEGATIVE STRAND VIRUSES 2000. 11TH INTERNATIONAL CONFERENCE ON NEGATIVE STRAND VIRUSES

Québec City, Québec, Canada
24–29 June 2000

CONTACT: Negative Strand Virus 2000 Conference, PO Box 33799, Decatur, GA 30033-0799, USA (Fax +1 404 728 0032; e-mail nsv2000@aol.com; http://www.nsv2000.com)

july 2000

INTRODUCTION TO DNA BIOINFORMATICS. A ONE-DAY PRACTICAL COMPUTER COURSE

University of Hertfordshire, Hatfield, 4 July 2000

INTRODUCTION TO PROTEIN BIOINFORMATICS. A ONE-DAY PRACTICAL COMPUTER COURSE

University of Hertfordshire, Hatfield, 5 July 2000

CONTACT: Dr Henry Brzeski, Dept of Biosciences, University of Hertfordshire, College Lane, Hatfield, Herts AL10 9AB (Tel. 01707 284554; Fax 01707 286137; e-mail h.brzeski@herts.ac.uk; http://www.herts.ac.uk/natsci/STC)

RNA EXTRACTION AND ANALYSIS. A ONE-DAY LABORATORY/LECTURE COURSE

University of Hertfordshire, Hatfield, 6 July 2000

PCR METHODS AND APPLICATIONS. A ONE-DAY LABORATORY/LECTURE COURSE

University of Hertfordshire, Hatfield, 7 July 2000

CONTACT: Dr Ralph Rapley, Dept of Biosciences, University of Hertfordshire, College Lane, Hatfield, Herts AL10 9AB (Tel. 01707 285097; Fax 01707 286137; e-mail r.rapley@herts.ac.uk; http://www.herts.ac.uk/natsci/STC)

THE AMERICAN SOCIETY FOR VIROLOGY 19TH ANNUAL SCIENTIFIC MEETING (SPONSOR: COLORADO STATE UNIVERSITY)

Fort Collins, Colorado
8–12 July 2000

CONTACT: Sidney E. Grossberg, Secretary-Treasurer, American Society for Virology, Department of Microbiology and Molecular Genetics, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI53226-0509 (Tel. +1 414 456 8104; Fax+1 414 456 6566; e-mail segrossb@mcw.edu)

ANAEROBE 2000. CONGRESS OF THE CONFEDERATION OF ANAEROBE SOCIETIES

Manchester, 10–12 July 2000

CONTACT: Anaerobe Society of the Americas, PO BOX 452058, Los Angeles, CA 90045, USA (Fax +1 310 216 9274; e-mail asa@anaerobe.org; http://www.anaerobe.org)

TECHNIQUES IN MEDICAL MOLECULAR BIOLOGY. A THREE-DAY LABORATORY/LECTURE COURSE

University of Hertfordshire, Hatfield, 12–14 July 2000

CONTACT: Dr Ralph Rapley, Dept. of Biosciences, University of Hertfordshire, College Lane, Hatfield, Herts AL10 9AB (Tel. 01707 285097; Fax 01707 286137; e-mail r.rapley@herts.ac.uk; http://www.herts.ac.uk/natsci/STC)

BEYOND THE GENOME. 18TH INTERNATIONAL CONGRESS OF BIOCHEMISTRY AND MOLECULAR BIOLOGY

International Conference Centre, Birmingham
16–20 July 2000

CONTACT: Andrea Buxton, Centre Exhibitions, The NEC, Birmingham B40 1NT (Tel. 0121 767 3755; Fax 0121 767 3535; e-mail genome@necgroup.co.uk)

august 2000

ISR2000. 3RD INTERNATIONAL SYMPOSIUM ON *RHIZOCTONIA*

National Chung Hsing University, Taichung, Taiwan (ROC)
17–20 August 2000

CONTACT: Symposium Secretariat, College of Life Science, National Chung Hsing University, 250 Kuokuang Road, Taichung 402, Taiwan (Tel. +886 4 2840370; Fax +886 4 2860164; e-mail isr2000@dragon.nchu.edu.tw; http://www.nchu.deu.tw/~isr2000/)

BACILLUS 2000. APPLICATIONS AND SYSTEMATICS OF *BACILLUS* AND RELATIVES

Bruges, Belgium
30–31 August 2000

CONTACT: Dr Roger Berkeley, University of Bristol, Badock Hall, Stoke Park Road, Bristol BS9 1JQ (Tel. 0117 903 2480; Fax 0117 903 2499)

september 2000

ACINETOBACTER 2000: 5TH INTERNATIONAL SYMPOSIUM ON THE BIOLOGY OF *ACINETOBACTER*

Noordwijkerhout, The Netherlands
3–6 September 2000

CONTACT: Dr L. Dijkshoorn, Dept of Medical Microbiology, Academisch Ziekenhuis, Postbus 9600, 2300 RC Leiden, The Netherlands (Tel. +31 71 5263931; Fax +31 71 5248148; e-mail dijkshoorn@rullf2.medfac.leidenuniv.nl)

EXTREMOPHILES 2000. THE 3RD INTERNATIONAL CONGRESS ON EXTREMOPHILES

Technical University Hamburg-Harburg, Germany
3–7 September 2000

CONTACT: Ms Gerlinde Loebkens, TUHH-Technologie GmbH, Schellerdamm 4, 21079 Hamburg, Germany (Tel. +49 40 76618012; Fax +49 40 76618018; e-mail loebkens@tutech.de)

ICHC 2000. XITH INTERNATIONAL CONGRESS OF HISTOCHEMISTRY AND CYTOCHEMISTRY

University of York
3–8 September 2000

CONTACT: Allison Winton, Publicity Officer, Royal Microscopical Society, 37/38 St Clements, Oxford OX4 1AJ (Tel. 01865 248768; Fax 01865 791237; Conference e-mail rebecca@rms.org.uk; Exhibition e-mail allison@rms.org.uk; http://www.rms.org.uk; http://www.med.ic.ac.uk/external/ichc_2000/)

Comment

Doomed to live in interesting times

This summer (1999) I had to return funding for a studentship in bioinformatics to the Biotechnology and Biological Sciences Research Council (BBSRC) because I was unable to find a suitable candidate. There was considerable interest from within Europe, particularly Italy, and from the USA, but BBSRC rules specify that applicants must be UK residents. The reason for writing about this here is that I have discovered that I am not alone in facing this problem.

The shortage of trained bioinformatics staff throughout the UK is well known. A review of the likely needs of the UK academic and private sector conducted by BBSRC in 1998 revealed that there was a significant shortfall in the number of bioinformaticians currently required at a variety of levels and that this problem was likely to get worse. As a result, BBSRC has proposed supporting two summer schools in bioinformatics. It has increased the number of places sponsored on bioinformatics-related masters courses by 60 %. Through the Bioinformatics Initiative BBSRC also funds 12 studentships each year and the Engineering & Physical Sciences Research Council (EPSRC) funds three.

The research projects funded through the Initiative usually provide support for one or more research assistants (RA), and BBSRC experience has shown that RA positions in bioinformatics are harder to fill than those in other areas of biology. It is often difficult recruiting someone with expertise in both biology and computing. Out of 44 grants surveyed, 18 grantholders experienced a delay of 6 months or more from the date of announcement of the grant to the RA starting work. In eight of these cases the delay was so great that the grantholders approached BBSRC for an extension to the grant to allow them more time to appoint someone.

Retaining the RA for the duration of the grant is also a problem. Of the 44 grants, eight (so far) have seen the original RA resign (usually to take up a permanent or more lucrative job) and finding a successor, where possible, has taken several months. As a grant progresses, of course, it becomes more and more difficult to find a replacement RA who can come up to speed in time to deliver the original project objectives. In addition, contracts of less than 3 years' duration are not particularly attractive.

Other research councils have also conducted surveys. EPSRC have focused on PhD students to determine the 'health of the discipline' and their report confirms what has been known anecdotally for some time, that in the field of Information Technology and Computer Science, it '*has become difficult to attract high-calibre students into PhD work*'. Not only do a lack of long-term career opportunities in universities and low pay act as barriers, but graduates emerging from university burdened by substantial debts are unlikely to pursue a comparatively poorly paid academic career. Pay levels in industry for the brighter graduates are currently set at three times the studentship award. Postgraduate students in the IT field also reported that they felt isolated from the real world and that there was insufficient contact with industry which would better prepare them for future employment.

The need for more people skilled in bioinformatics is clear to the Medical Research Council (MRC) too, who have just joined forces with the Particle Physics and Astronomy Research Council (PPARC) to launch Training Fellowships aimed at bioinformatics. The MRC does not have any evidence as yet of studentships being hard to fill. Could this be due to the extra £2,000 added to the stipend for bioinformatics? These additional funds are on top of a stipend already the highest amongst the research councils. Their venture is intended to encourage more people from fields other than biology to bring their talents to bear in analysing genomic information.

The shortage of bioinformaticians is also recognized outside the UK. In Germany, for instance, DFG (the German Science Foundation) has allocated DM 50 million over 5 years to fund three national centres for bioinformatics.

It is now accepted that the pace of data accumulation is increasing and that the interpretation and manipulation of information (especially genomic data) is crucial to the future of biological sciences. Bioinformatics skills are required urgently. The difficulties of recruitment and retention are exacerbating the situation. The needs of industry, especially pharmaceuticals, are driving up salaries. Industrial labs often have better facilities and working conditions too, and are able to offer a more stable career structure than the series of short-term contracts available in academia. Taken together this is making it practically impossible for academia to compete.

So, is this a new model for migration of a subject out of universities into the hands of industry? Will industry take responsibility for training? If it does not, who will? As the ancient Chinese curse would have it, we seem doomed to live in interesting times.

● ***Dave Roberts, Editor***

● Please note that views expressed in *Comment* do not necessarily reflect official policy of the SGM Council.